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Location (Bldg/Room#): _____

Scientific and Technical Information Center

SEARCH REQUEST FORM

Date: 11/4/2002 Requester's Full Name: Joyce Tung Examiner #: 73507

Art Unit: 1637 Phone (305) 7112 Serial Number: 09/880,377

Results Format Preferred (circle): PAPER DISK E-MAIL 10801

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To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Date: _____

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known.

For Sequence Searches Only *Please include all pertinent information (parent, grandchild, divisional, or issued patent numbers) along with the appropriate serial number.*

please search chemical structure in claim 13.

Thank you.

mail room No. 10801

POINT OF CONTACT:
PAUL SCHULWITZ
TECHNICAL INFO. SPECIALIST
CM1 6B06 TEL. (703) 305-1954

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STAFF USE ONLY

Searcher: _____

Searcher Phone #: _____

Searcher Location: _____

Date Searcher Picked Up: 11/4

Date Completed: 11/6

Searcher Prep & Review Time: 10

Online Time: 7

Type of Search

_____ NA Sequence (#)

_____ AA Sequence (#)

1 Structure (#)

_____ Bibliographic

_____ Litigation

_____ Fulltext

_____ Other

Vendors and Cost

18.5 STN _____ Dialog

_____ Questel/Orbit _____ Dr.Link

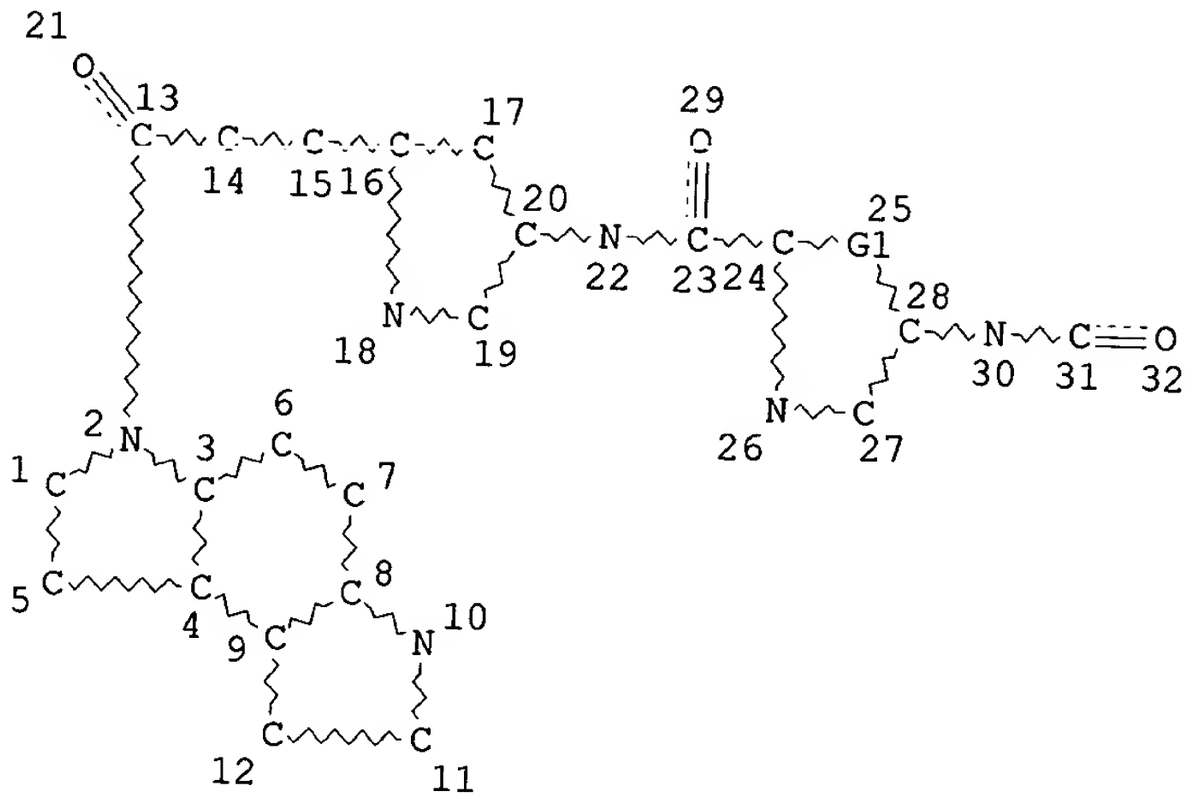
_____ Lexis/Nexis _____ Westlaw

_____ WWW/Internet

_____ In-house sequence systems (list)

_____ Other (specify)

=> d que
L1 STR



VAR G1=C/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
L3 30 SEA FILE=REGISTRY SSS FUL L1
L4 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

=> d ibib abs hitstr 1-9

L4 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833321 HCAPLUS
DOCUMENT NUMBER: 135:371743
TITLE: Preparation of pyrrole-imidazole polyamide-duocarmycin segment conjugates as interstrand crosslinking agents for DNA in cancer treatment
INVENTOR(S): Sugiyama, Hiroshi; Bando, Toshikazu; Iida, Hirokazu; Saito, Isao
PATENT ASSIGNEE(S): Japan Science and Technology Corporation, Japan
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001085733 A1 20011115 WO 2001-JP3756 20010501
W: US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
JP 2001322992 A2 20011120 JP 2000-140361 20000512
PRIORITY APPLN. INFO.: JP 2000-140361 A 20000512
OTHER SOURCE(S): MARPAT 135:371743
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. represented by the following general formula A-L-B-X-B-L-A (I; wherein B represents a chem. structure capable of recognizing a base sequence of a DNA; A represents a chem. structure capable of binding to one of the bases of the DNA; L represents a linker by which the chem. structures A and B can be linked to each other; and X represents a spacer by which the A-L-B components can be linked to each other), by which two DNA strands can be interstrand-crosslinked, are prepd. Also claimed are a method of interstrand-crosslinking DNA by using these compds. and medicinal compns. contg. interstrand crosslinking agents of DNA. In the compds. I, the above chem. structure capable of recognizing a base sequence of a DNA is derived from pyrrole and/or imidazole and the chem. structure capable of binding to one of the bases of the DNA possesses a cyclopropane ring. More specifically, the compds. represented by N-[3-[4-(N-methylimidazol-2-ylcarbonylamino)-N-methylpyrrol-2-yl]acryloyl]cyclopropa[c]pyrrolo[3,2-e]indole derivs. (pyrrole-imidazole polyamide-duocarmycin segment conjugates) [II; X = CO, COCH:CHCO, CO(CH2)4CO, CO-p-C6H4-CO] are prepd. The B component in the compds. I, i.e. the 4-(N-methylimidazol-2-ylcarbonylamino)-N-methylpyrrole moiety of II, recognizes a DNA base sequence and is capable of specifically interstrand-crosslinking to the specific base sequence of DNA. These compds. inhibit the replication of DNA by interstrand-crosslinking to DNA and thereby are useful for the treatment of cancer. Interstrand-crosslinking reaction of the compds. II to DNA oligomers was examd. using polyacrylamide gel electrophoresis. For example, it was confirmed that II [X = CO(CH2)4CO] interstrand-crosslinked to the TGGC or GCCA or its complimentary sequence of DNA, in particular in the copresence of a triamide (III; X = Y = N and Z = CH; X = Y = Z = N; X = N and Y = Z = CH; X = Z = CH and Y = N).

IT **373362-22-2P 373362-24-4P 373362-26-6P**
373362-27-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrrole-imidazole polyamide-duocarmycin conjugates as DNA interstrand crosslinking agents for treatment of cancer)

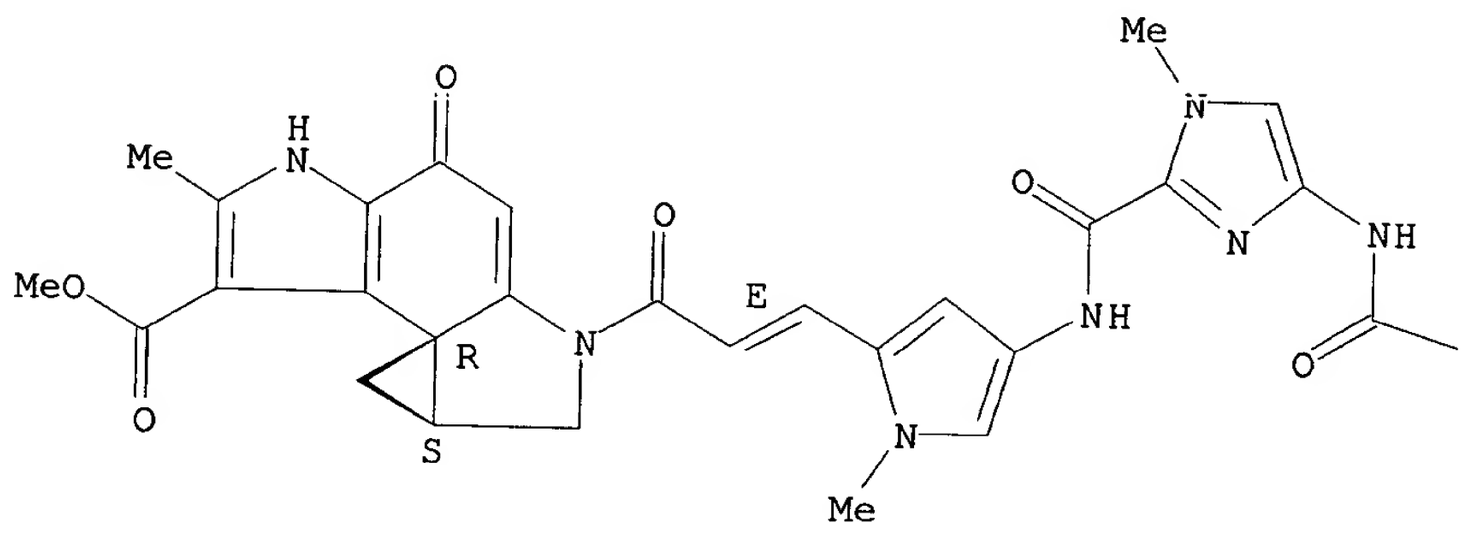
RN 373362-22-2 HCAPLUS

CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2,2'-[(1,6-dioxo-1,6-hexanediyl)bis[imino(1-methyl-1H-imidazole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)[(2E)-1-oxo-2-propene-3,1-diyl]]]bis[1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, dimethyl ester, (7bR,7'bR,8aS,8'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



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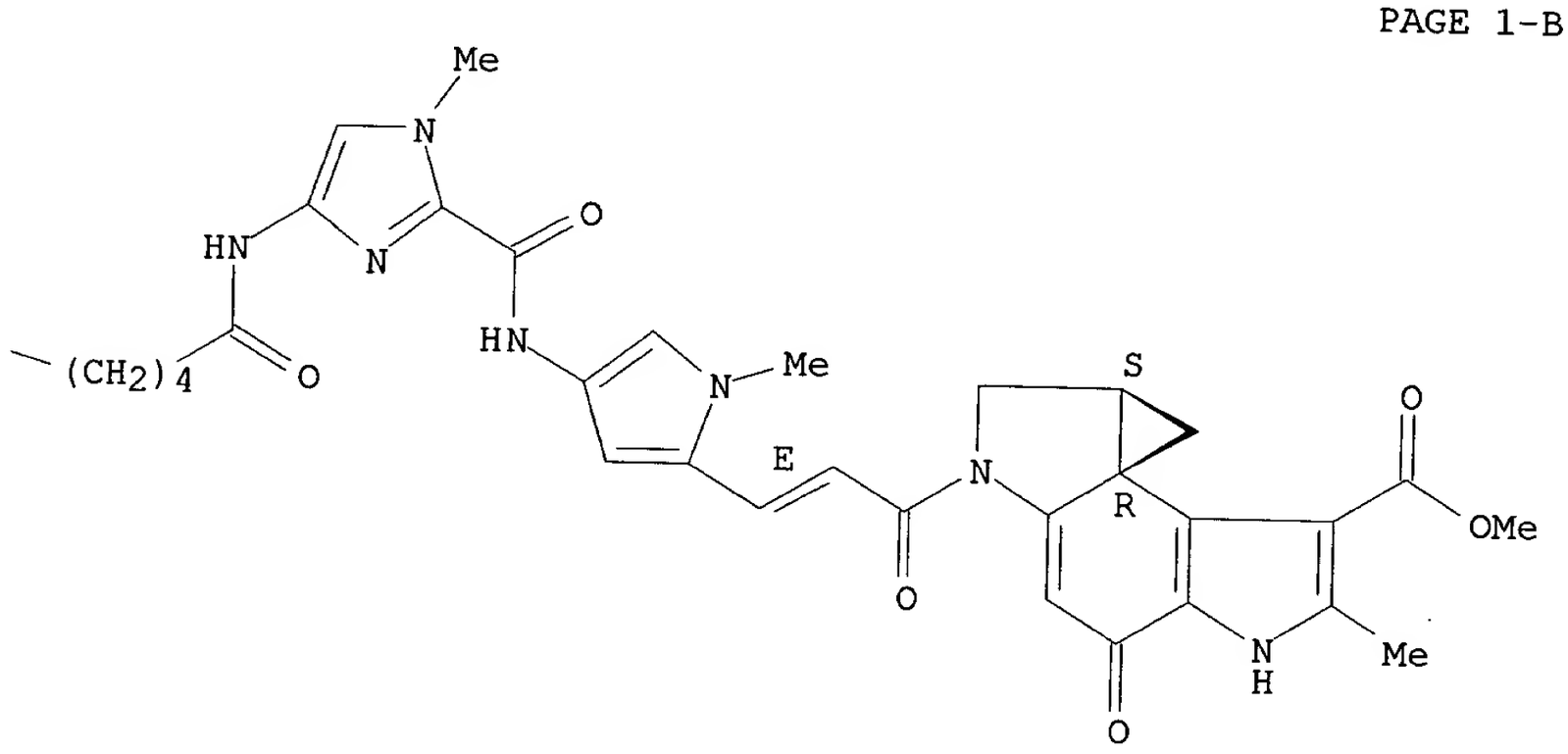

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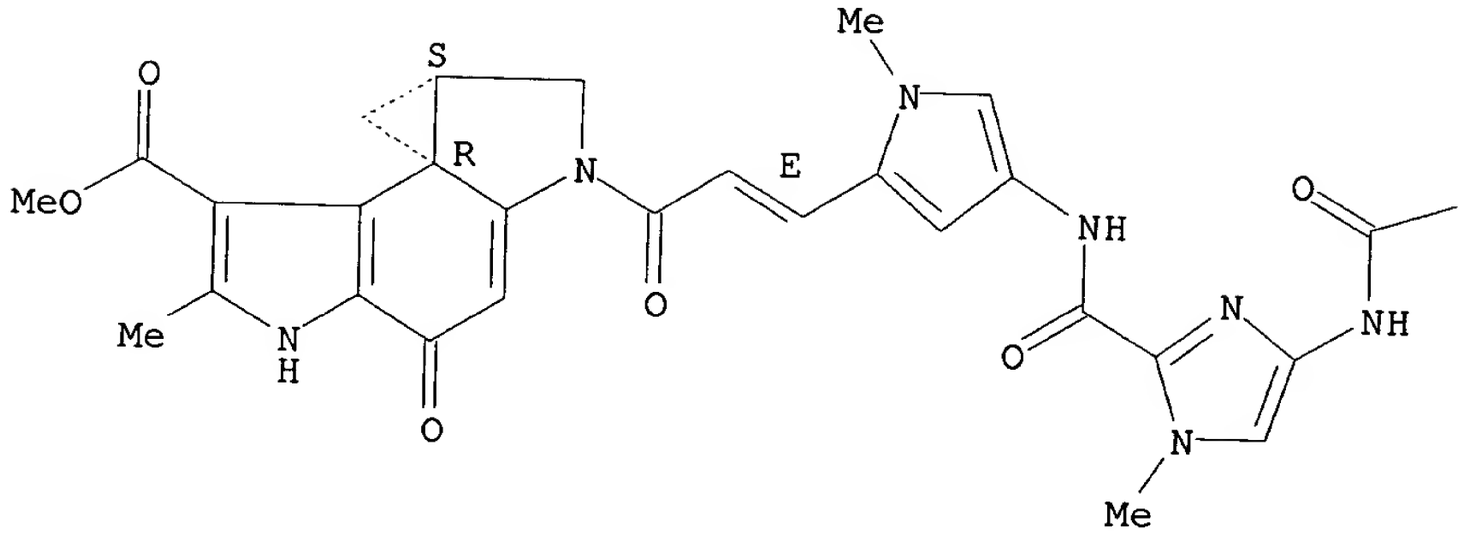
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2,2'-[1,4-phenylenebis[carbonylimino(1-methyl-1H-imidazole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)[(2E)-1-oxo-2-propene-3,1-diyl]]]bis[1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, dimethyl ester, (7bR,7'bR,8aS,8'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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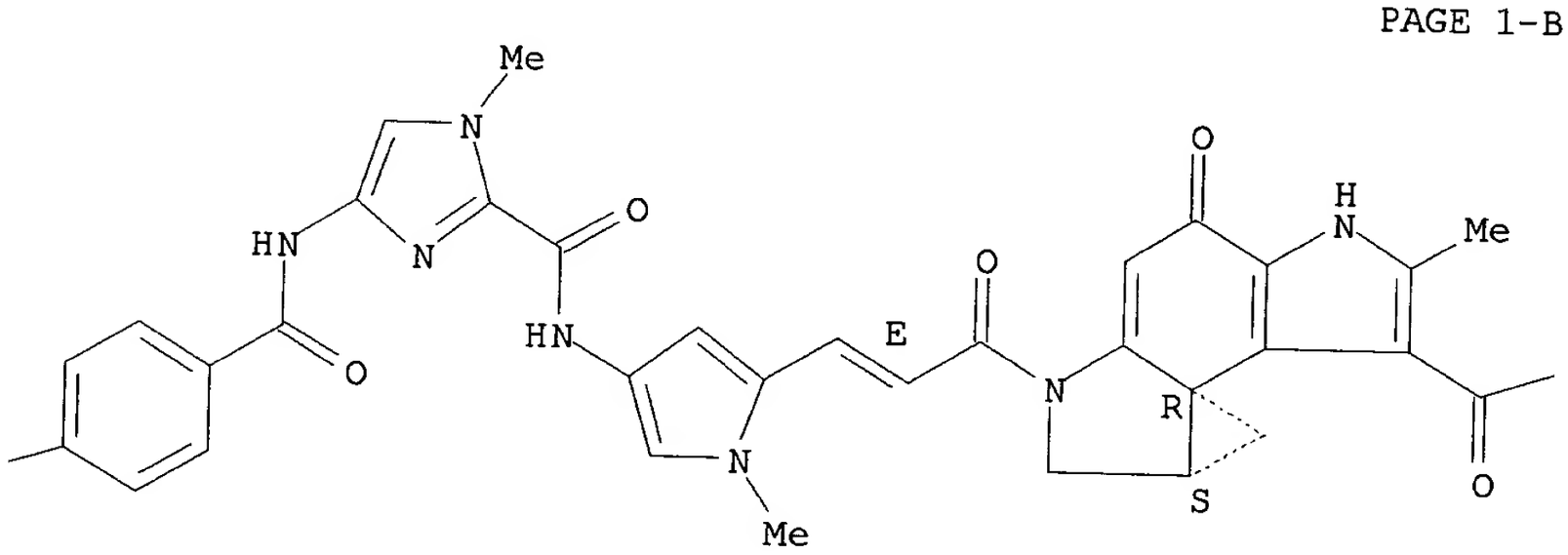


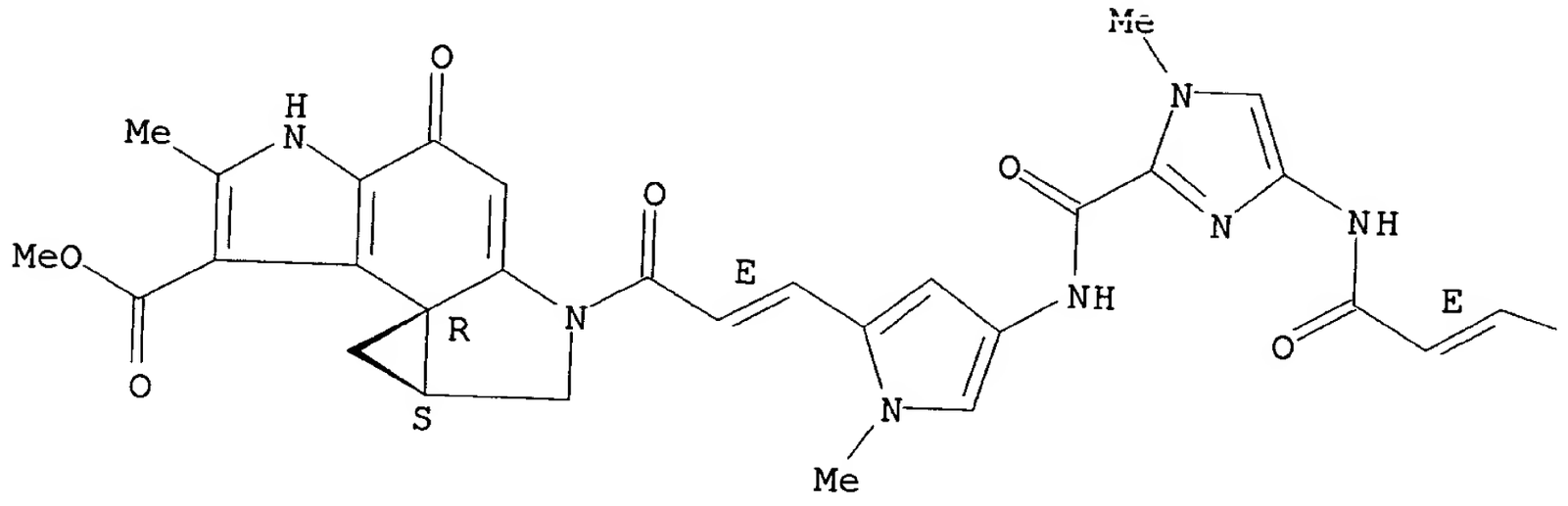
PAGE 1-C

—OMe

RN 373362-26-6 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2,2'-[(1,4-dioxo-2-butene-1,4-diyl)bis[imino(1-methyl-1H-imidazole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)[(2E)-1-oxo-2-propene-3,1-diyl]]]bis[1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, dimethyl ester, (7bR,7'bR,8aS,8'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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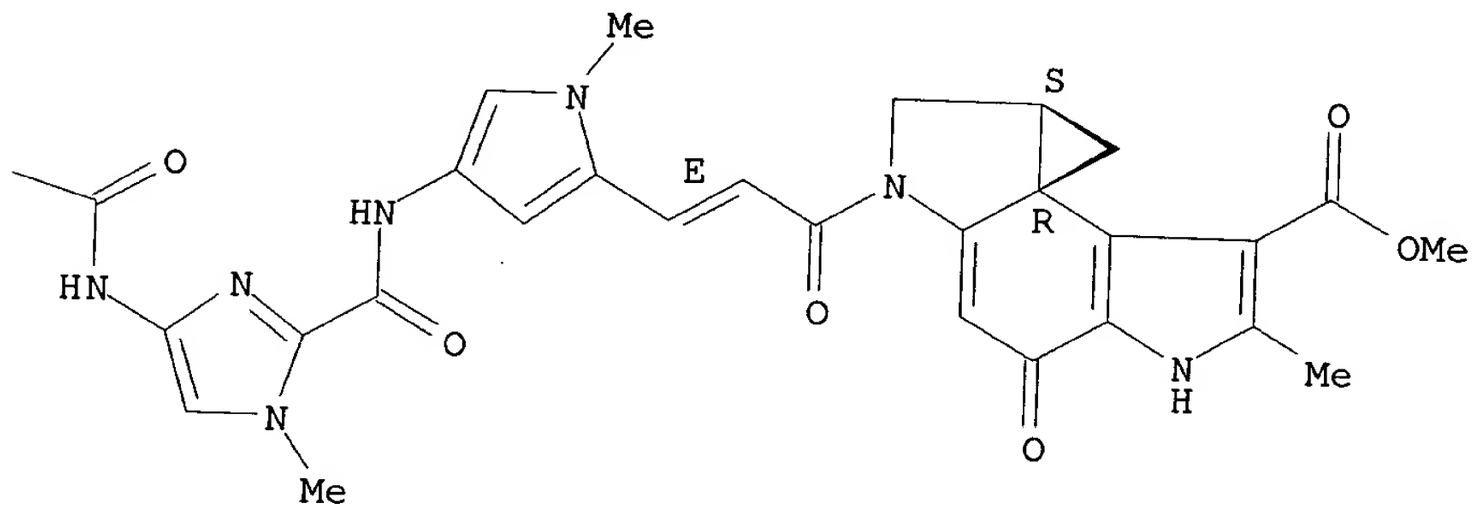
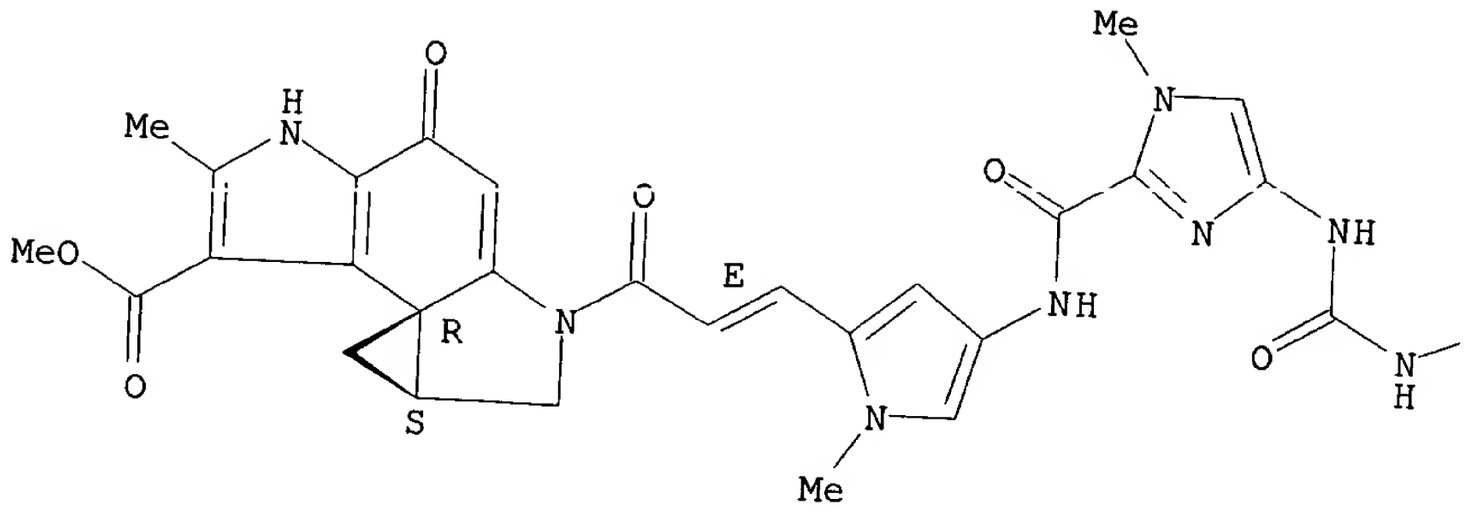


RN 373362-27-7 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2,2'-[carbonylbis[imino(1-methyl-1H-imidazole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)[(2E)-1-oxo-2-propene-3,1-diyl]]]bis[1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, dimethyl ester, (7bR,7'bR,8aS,8'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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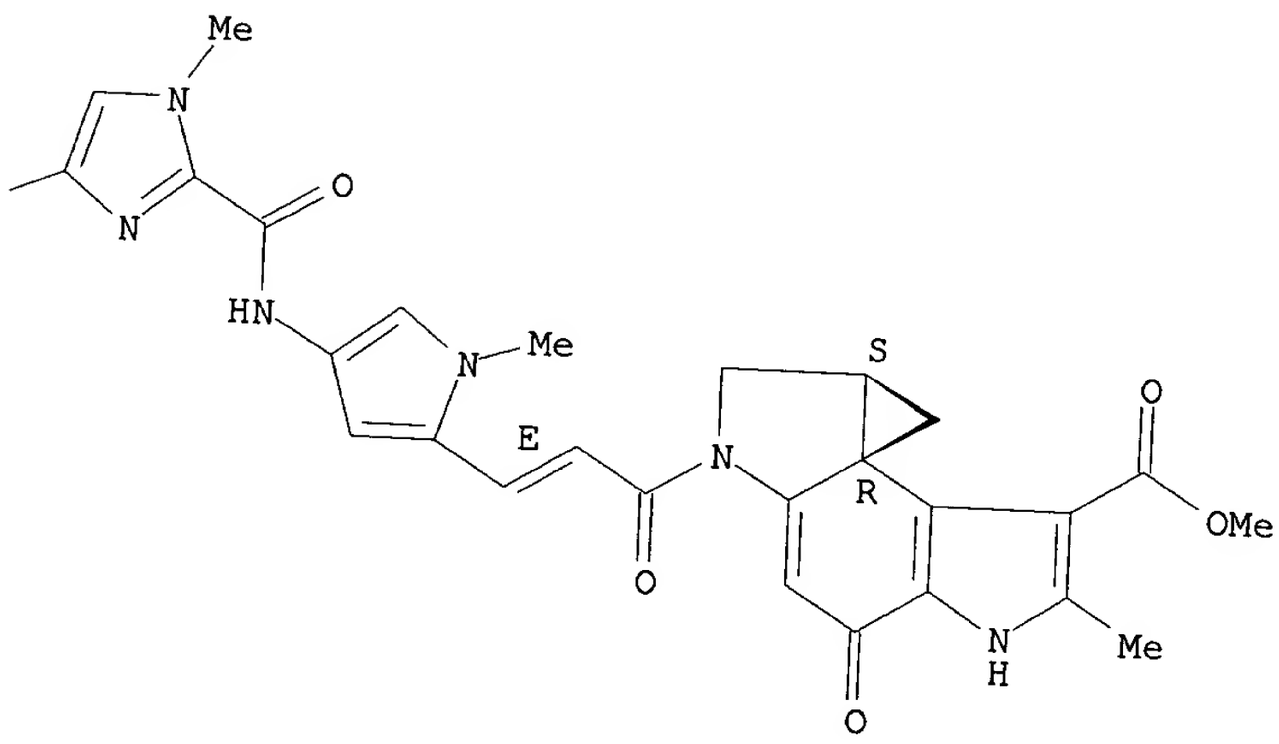


REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:365880 HCAPLUS
DOCUMENT NUMBER: 134:366795
TITLE: DNA sequence recognition by pyrrole-imidazole polyamide for use in anticancer drug screening
INVENTOR(S): Sugiyama, Hiroshi; Saito, Akira; Iida, Hirokazu
PATENT ASSIGNEE(S): Foundation for Scientific Technology Promotion, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001136974	A2	20010522	JP 1999-326007	19991116
WO 2001036677	A1	20010525	WO 2000-JP7992	20001113
W: US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1152061	A1	20011107	EP 2000-974961	20001113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

JP 1999-326007 A 19991116
WO 2000-JP7992 W 20001113

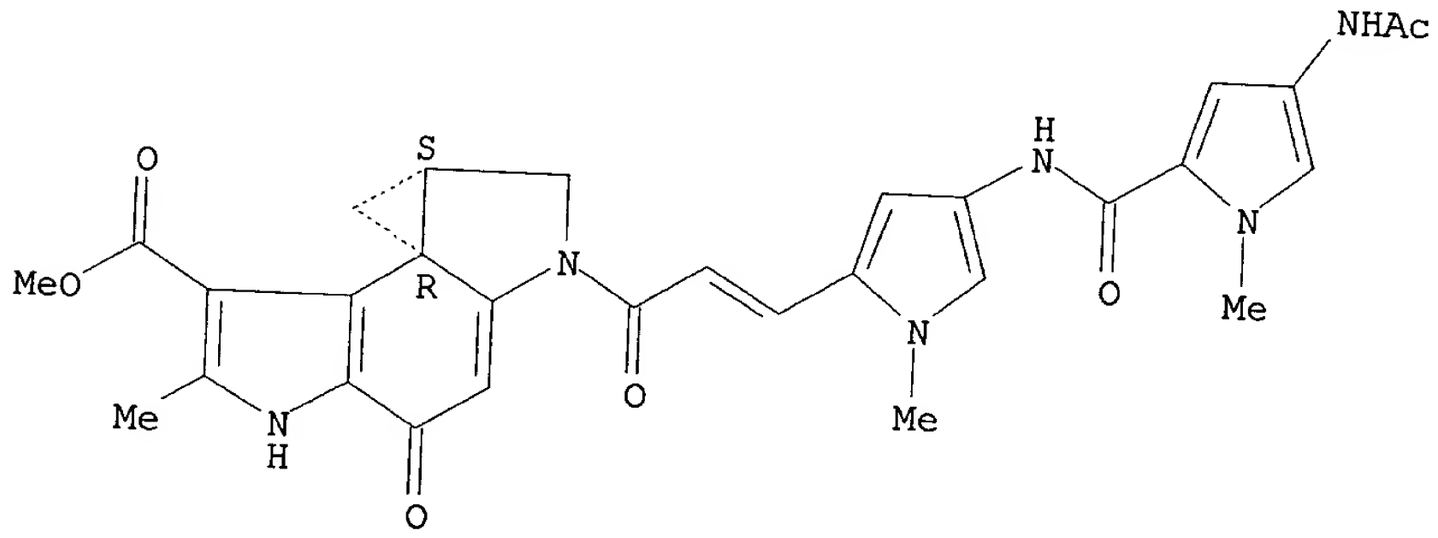
AB Novel chem. species represented by the following general formula B-L-A (B = a chem. structure capable of recognizing the base sequence of DNA, for example, optionally substituted pyrrole-imidazole polyamide; A = a chem. structure capable of binding to unnatural nucleotide bases, for example, the alkylation moiety of duocarmycin A; L = a linker capable of binding the chem. structures A and B, for example, vinyl) and use of those compds. in screening of biol. activity of chem. compds. are disclosed. Those compds. are preferably DNA alkylating agents, applicable as anticancer agents. Reagent kits for screening, including microtiter plates, are claimed. Drug screening using human cancer cell lines, CL-wt cells, HLC-2 cells, Jurkat cells, and HeLa cells, and synthetic scheme for the bioactive compds., are described.

IT **339984-88-2 339984-91-7**
RL: ARU (Analytical role, unclassified); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(DNA sequence recognition by pyrrole-imidazole polyamide for use in anticancer drug screening)

RN 339984-88-2 HCAPLUS

CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[3-[4-[[[4-(acetylamino)-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester, (7bR,8aS)- (9CI) (CA INDEX NAME)

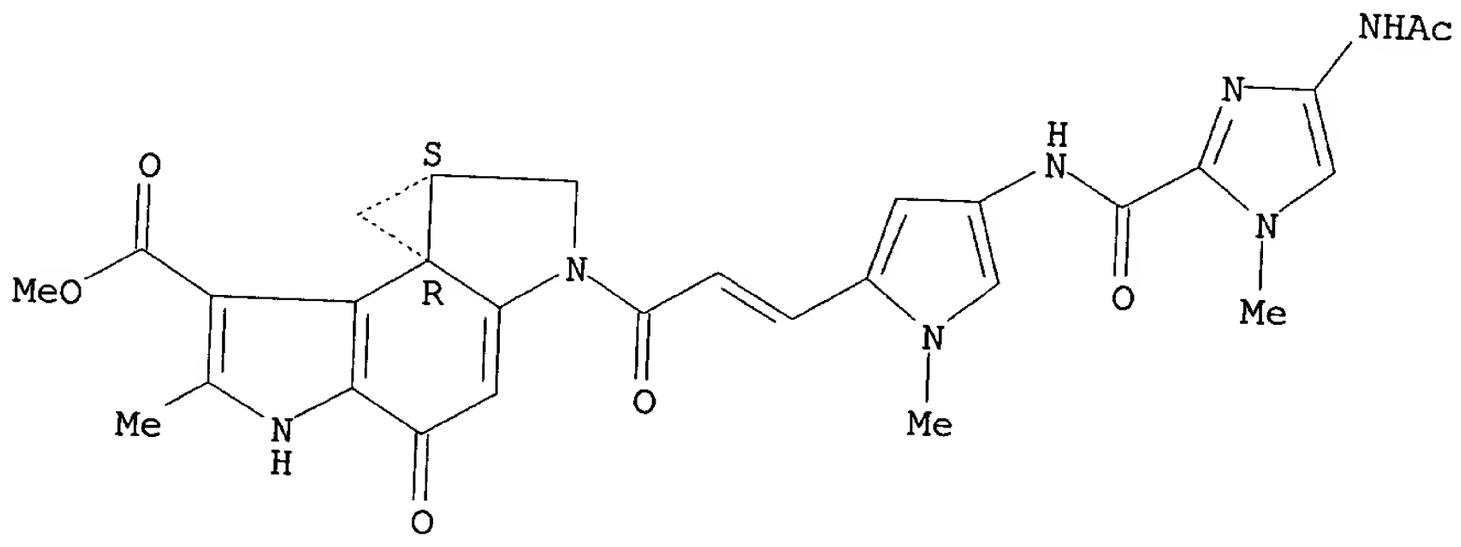
Absolute stereochemistry.
Double bond geometry unknown.



RN 339984-91-7 HCAPLUS

CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[3-[4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester, (7bR,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

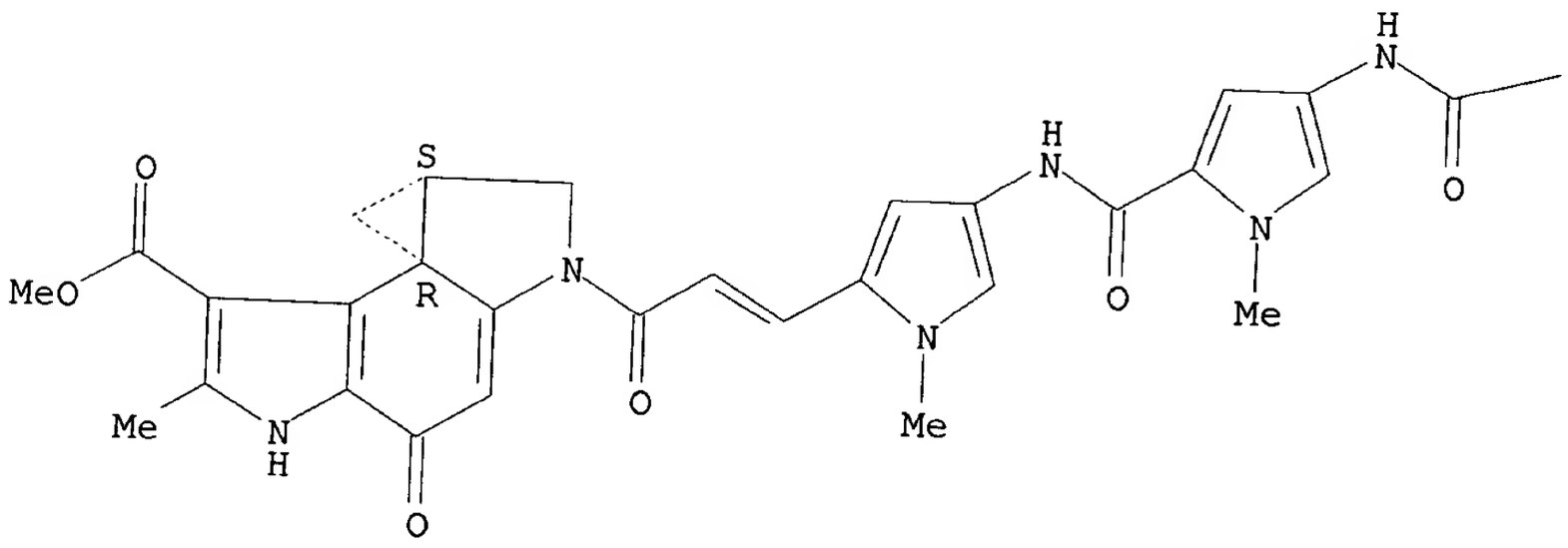


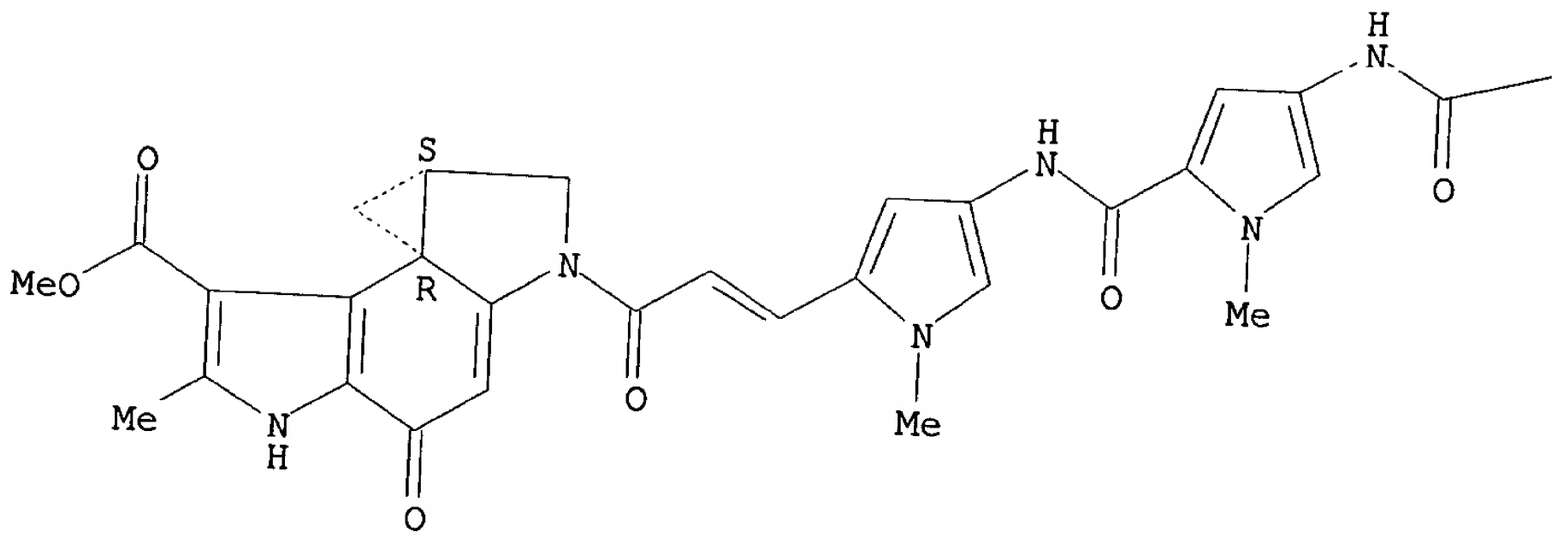
IT **339984-92-8P**
RL: ARU (Analytical role, unclassified); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(DNA sequence recognition by pyrrole-imidazole polyamide for use in anticancer drug screening)

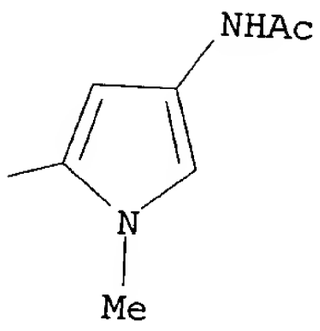
RN 339984-92-8 HCAPLUS

CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[3-[4-[[[4-[[[4-(acetylamino)-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester, (7bR,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.







L4 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:327062 HCAPLUS
DOCUMENT NUMBER: 135:102536
TITLE: Sequence-specific DNA interstrand cross-linking by imidazole-pyrrole CPI conjugate
AUTHOR(S): Bando, Toshikazu; Iida, Hirokazu; Saito, Isao; Sugiyama, Hiroshi
CORPORATE SOURCE: CREST Japan Science and Technology Corporation (JST) Japan Division of Biofunctional Molecules Institute of Biomaterials and Bioengineering Tokyo Medical and Dental University, Kanda Chiyoda Tokyo, 101-0062, Japan
SOURCE: Journal of the American Chemical Society (2001), 123(21), 5158-5159
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB DNA interstrand crosslinking inhibits both DNA replication and gene expression and therefore has considerable potential for mol. biol. and human medicine. However, an interstrand crosslinking agent that targets a predetd. base-pair sequence has not been achieved. Minor-groove binding polyamides that contain N-methylimidazole (Im)-N-methylpyrrole

(Py)hydroxypyrrole (Hp), which uniquely recognize each of the four Watson-Crick base pairs, can be used as novel recognition parts of sequence-specific DNA alkylating agents. We also demonstrated that Im/Py diamide-CPI conjugate with a vinyl linker, ImPyLDu86, alkylates double-stranded DNA at predetd. sequences through highly cooperative homodimer formation. Herein we describe the synthesis of a covalent dimer of ImPyLDu86 connected with various linkers and their DNA interstrand crosslinking abilities. In conclusion, we developed a novel DNA interstrand crosslinking agent, that crosslinked double strands only in the presence of ImImPy at a nine-base-pair sequence, 5'-PyGGC(T/A)GCCPu-3'. The present system will provide a promising approach for the design of novel sequence-specific DNA interstrand crosslinking agents. Targeting specific sequences in the human genome by such sequence-specific crosslinking agent would constitute a powerful gene-regulating tool. Further studies on the applicability of this novel class of crosslinking agents are currently in progress.

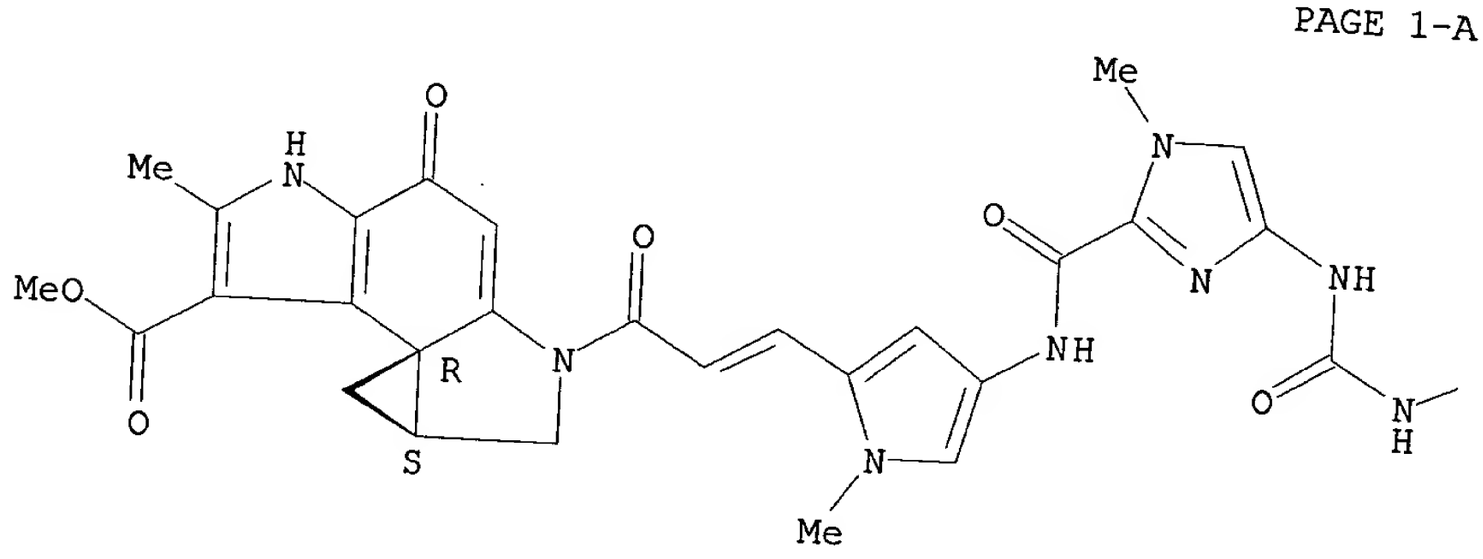
IT **349647-78-5 349647-79-6 349647-80-9**
349647-82-1 349647-83-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(sequence-specific DNA interstrand crosslinking by imidazole-pyrrole CPI conjugate)

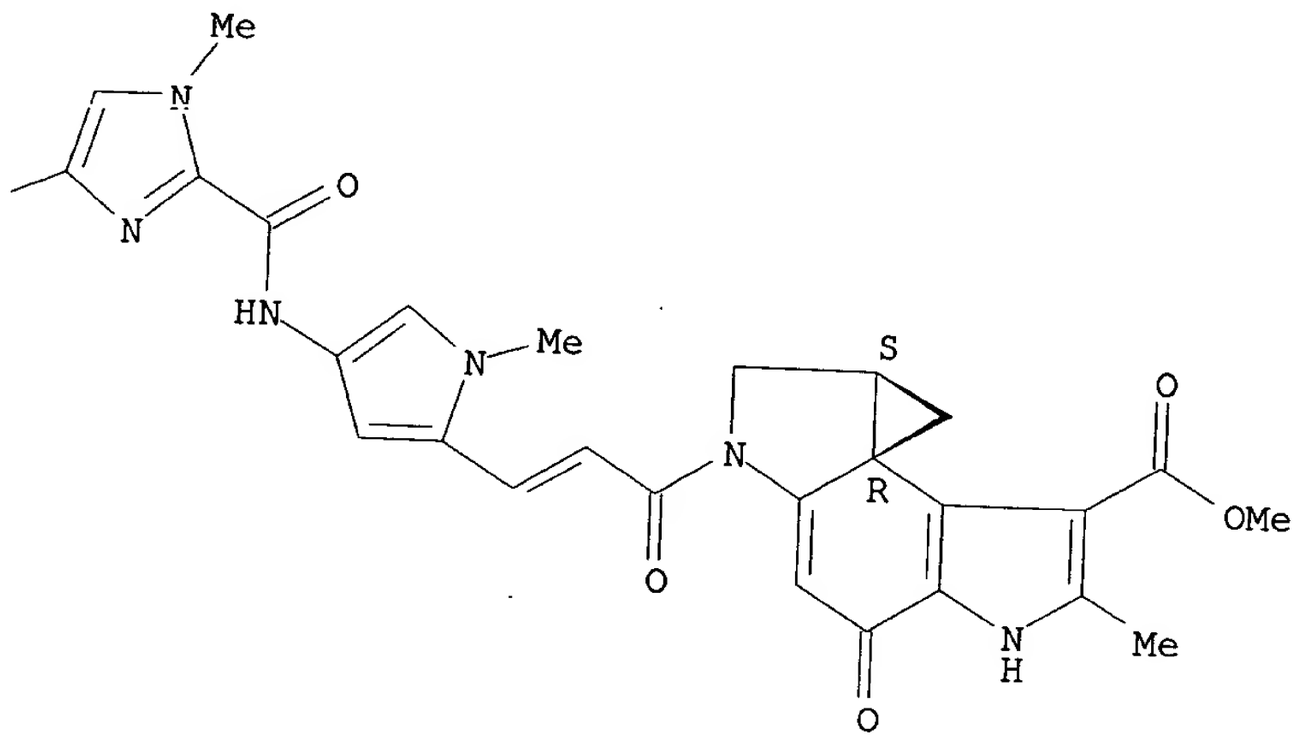
RN 349647-78-5 HCAPLUS

CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2,2'-[carbonylbis[imino(1-methyl-1H-imidazole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)(1-oxo-2-propene-3,1-diyl)]]bis[1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, dimethyl ester, (7bR,7'bR,8aS,8'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A





RN 349647-79-6 HCAPLUS

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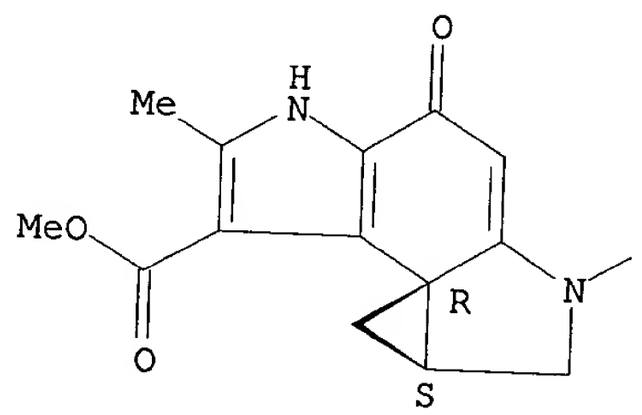
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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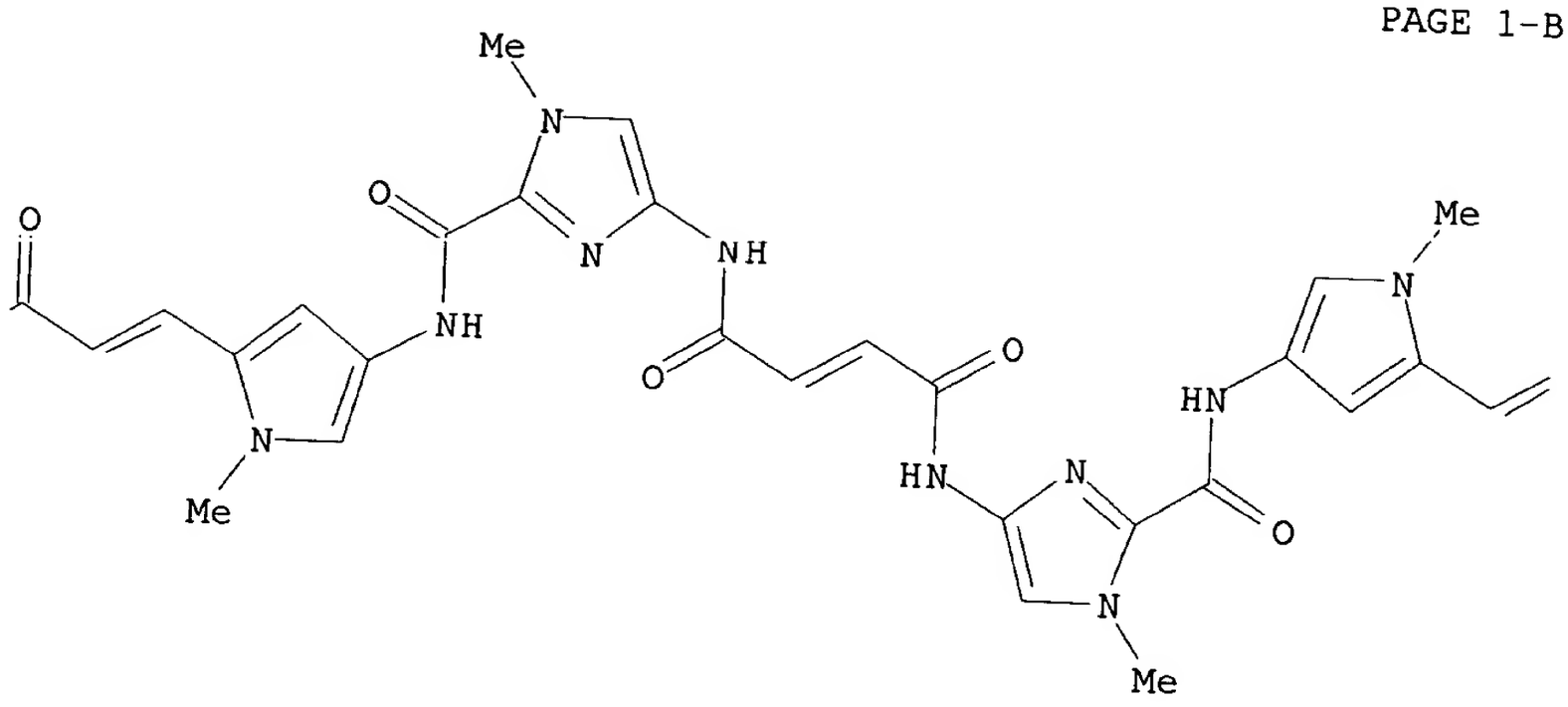

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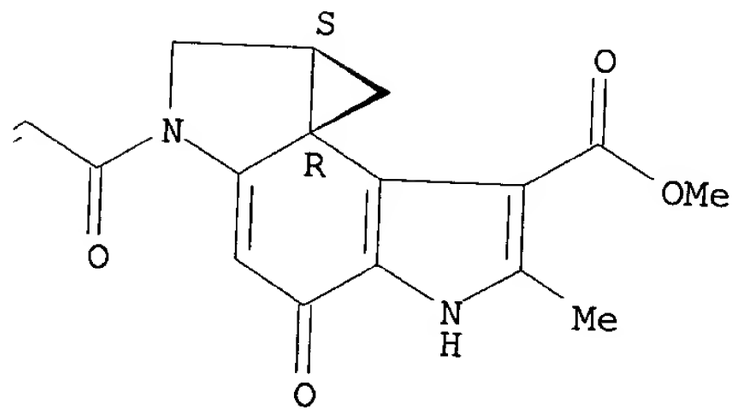

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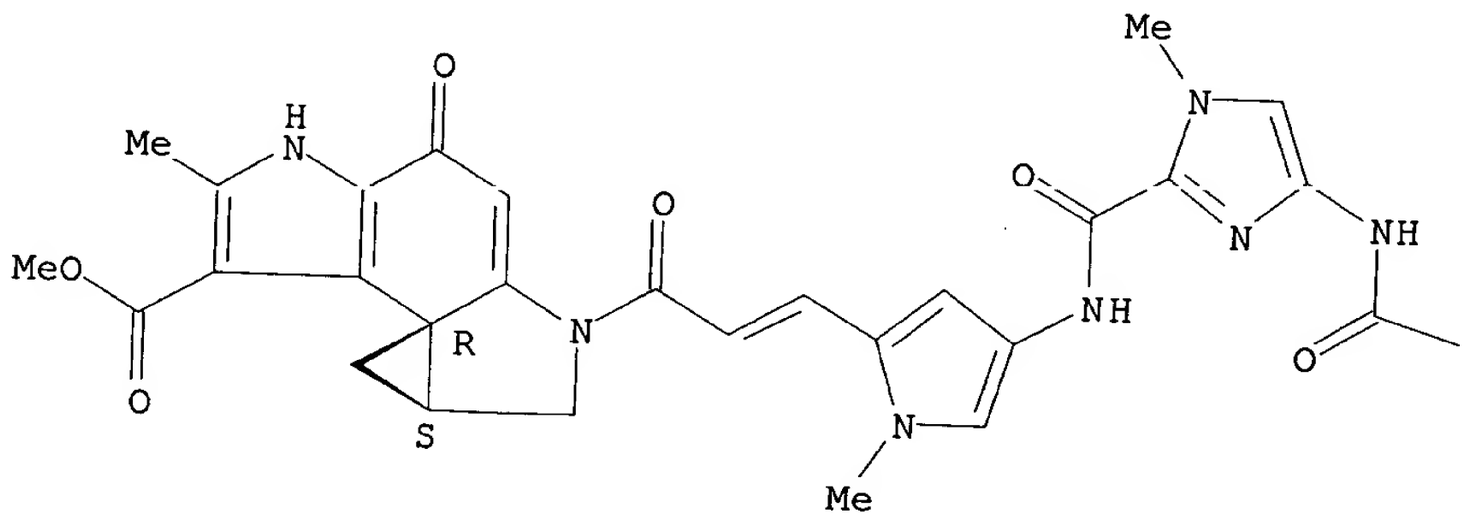
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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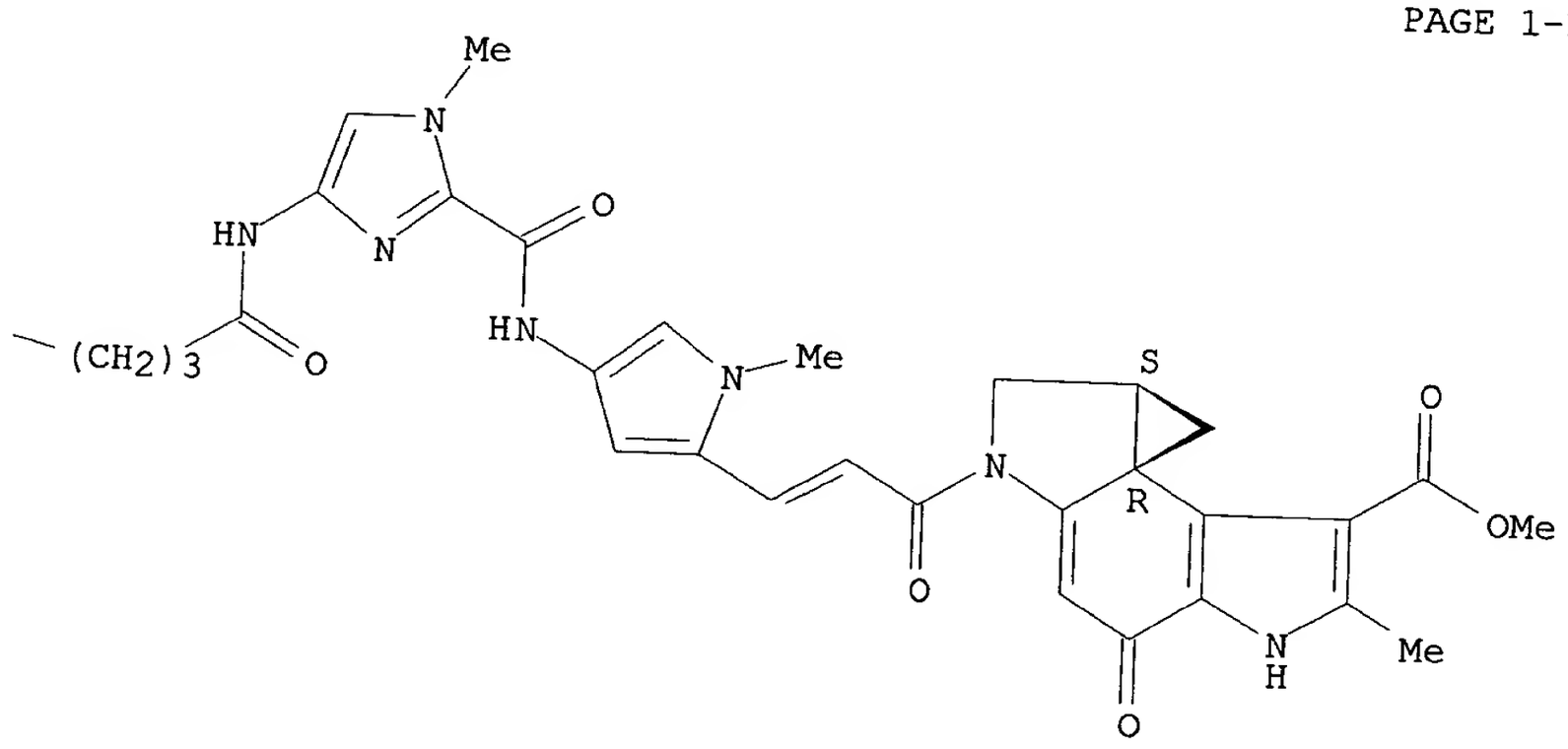
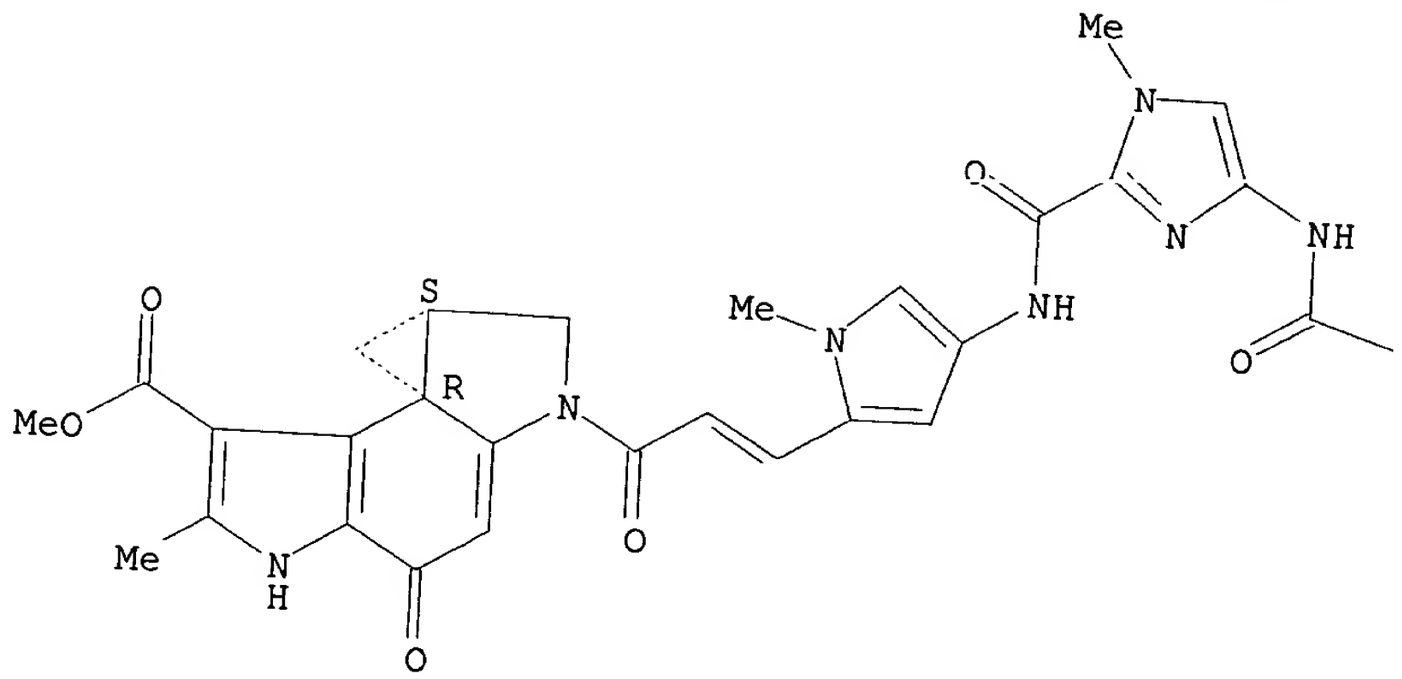


RN 349647-82-1 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2,2'-[1,3-phenylenebis[carbonylimino(1-methyl-1H-imidazole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)(1-oxo-2-propene-3,1-diyl)]]bis[1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, dimethyl ester, (7bR,7'bR,8aS,8'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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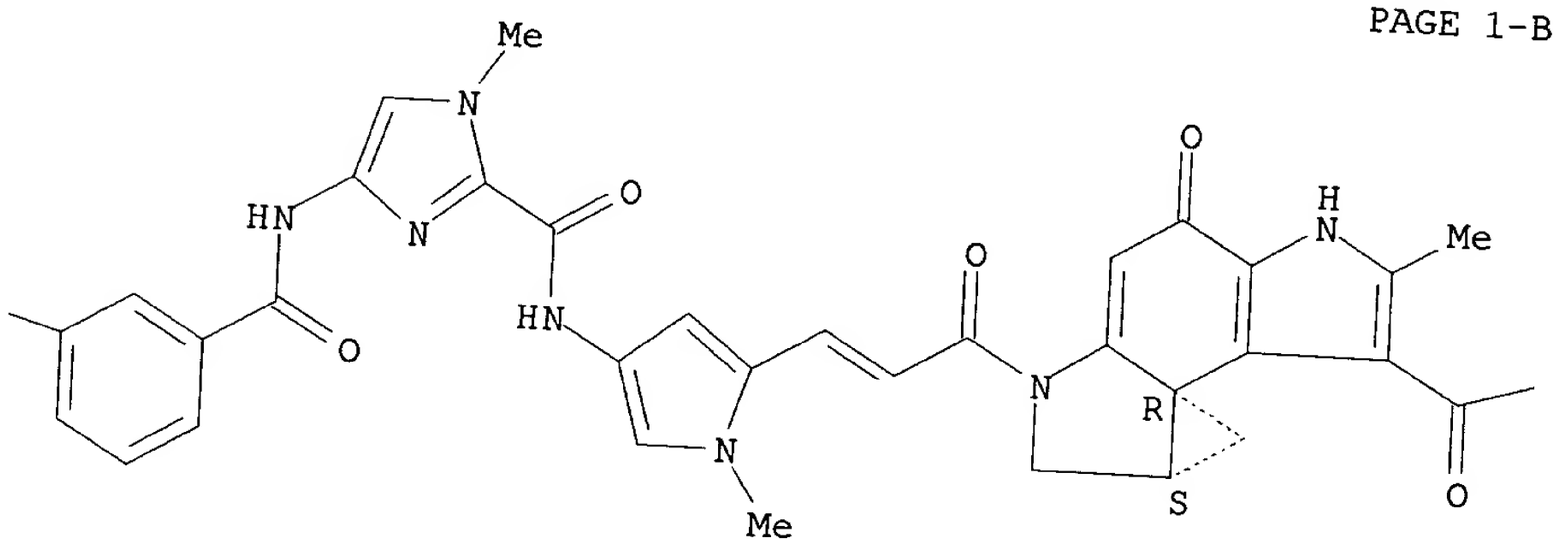


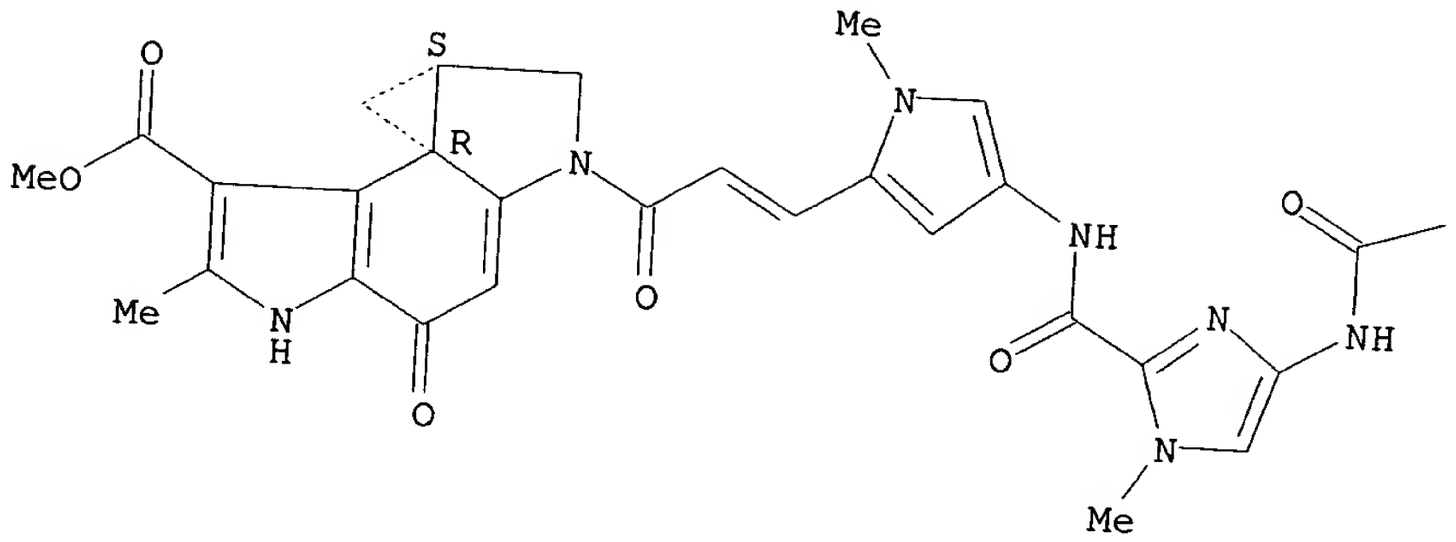
PAGE 1-C

—OMe

RN 349647-83-2 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2,2'-[1,4-phenylenebis[carbonylimino(1-methyl-1H-imidazole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)(1-oxo-2-propene-3,1-diyl)]]bis[1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, dimethyl ester, (7bR,7'bR,8aS,8'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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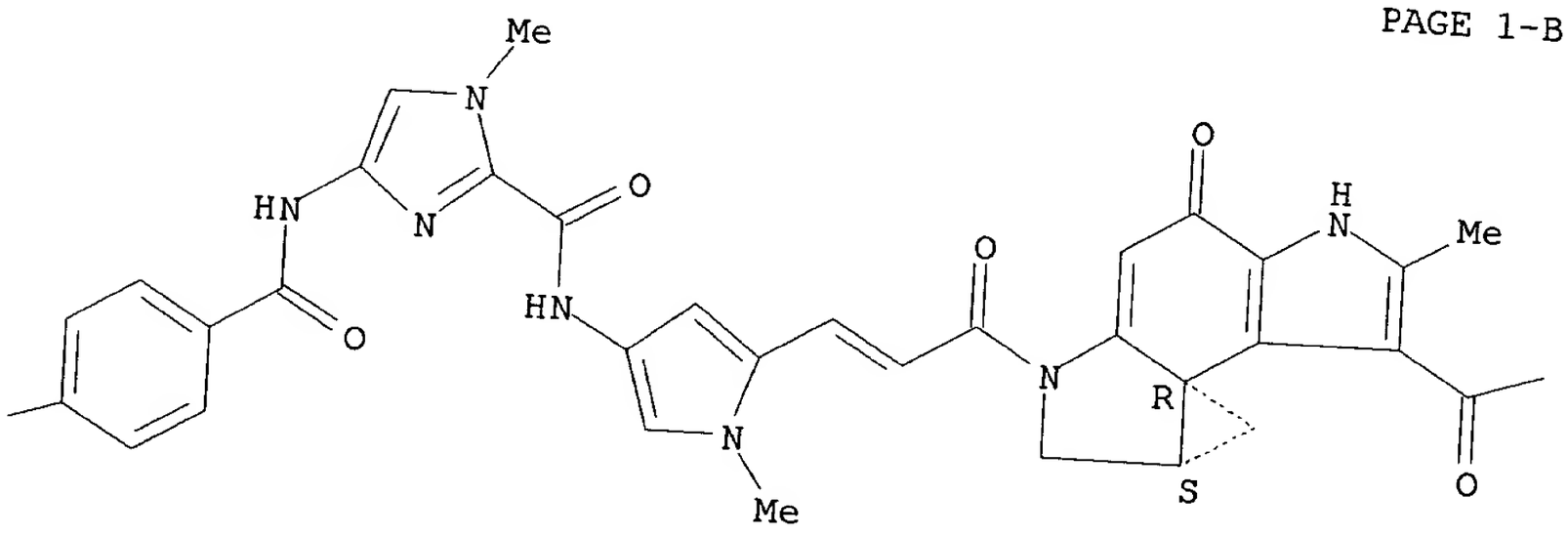


PAGE 1-C

—OMe

IT **349647-81-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological

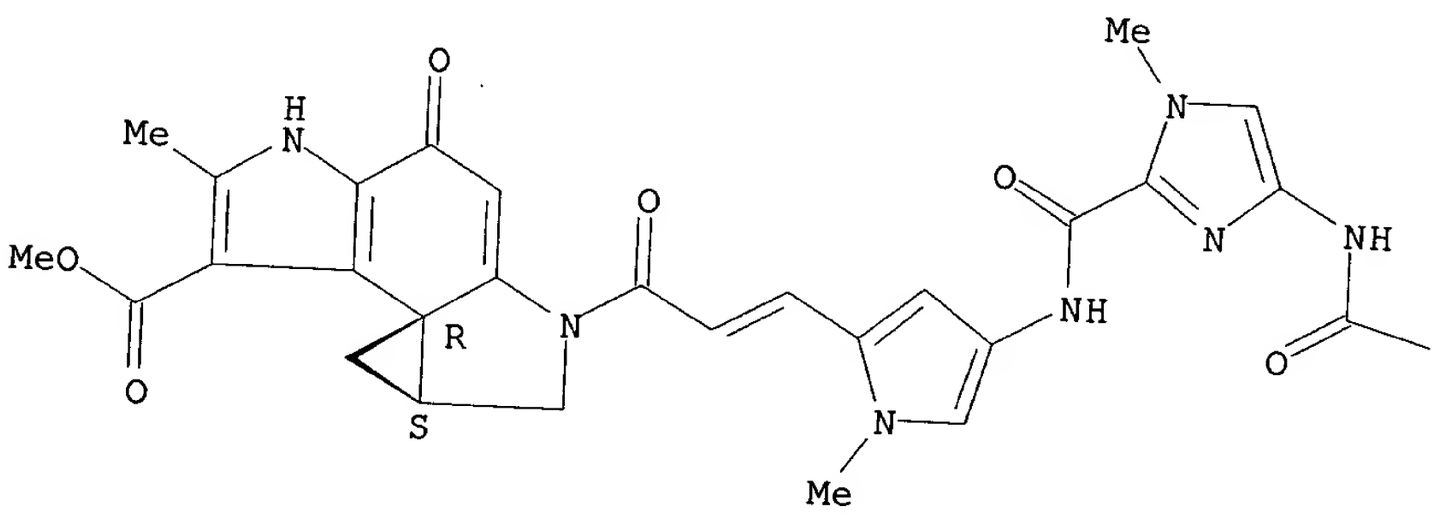
study); PREP (Preparation)
(sequence-specific DNA interstrand crosslinking by imidazole-pyrrole CPI conjugate)

RN 349647-81-0 HCAPLUS

CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2,2'-[(1,6-dioxo-1,6-hexanediyl)bis[imino(1-methyl-1H-imidazole-4,2-diyl)carbonylimino(1-methyl-1H-pyrrole-4,2-diyl)(1-oxo-2-propene-3,1-diyl)]]bis[1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, dimethyl ester, (7bR,7'bR,8aS,8'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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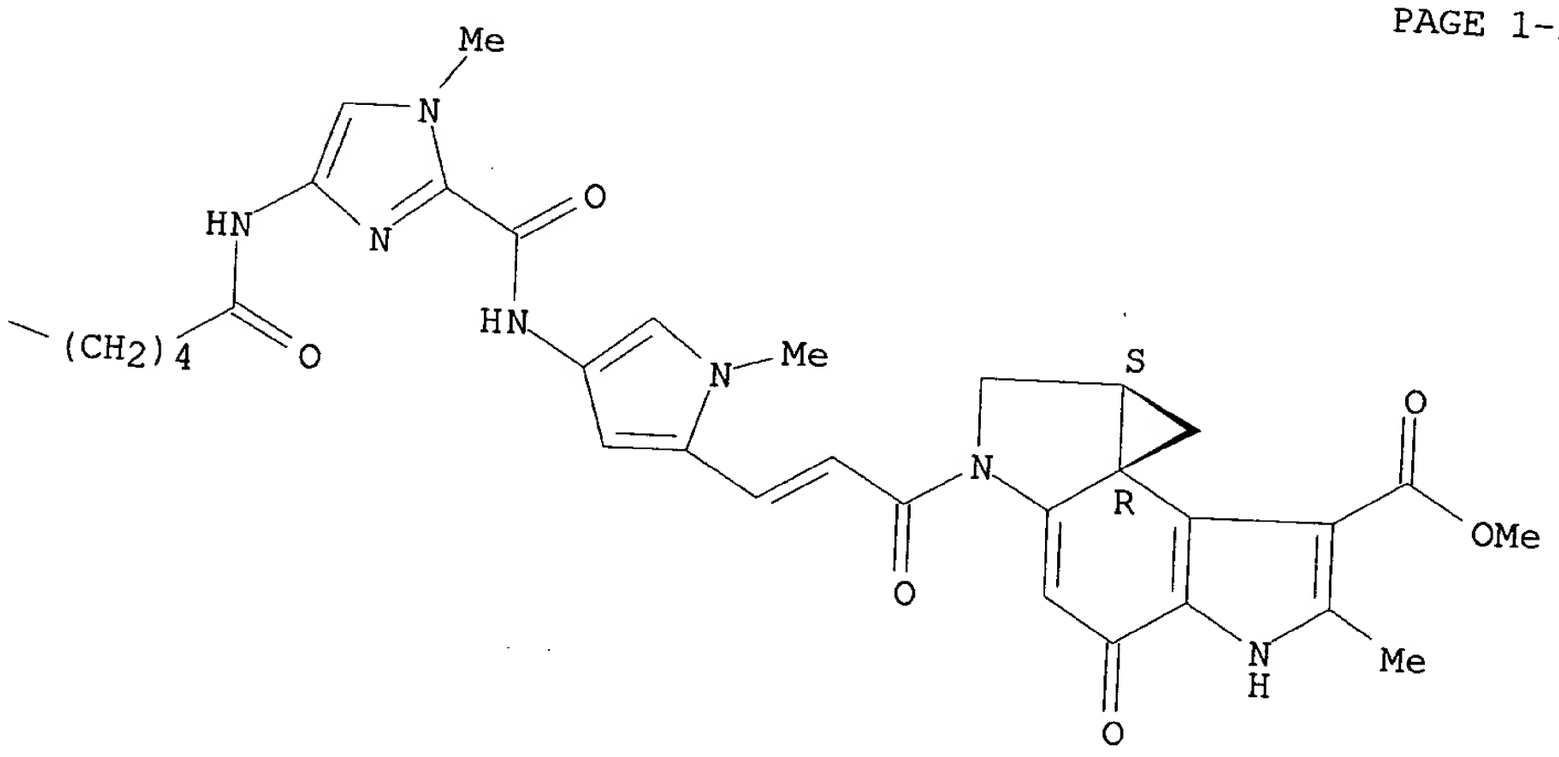


REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:707167 HCAPLUS
DOCUMENT NUMBER: 133:266852

TITLE: Preparation of duocarmycin derivatives capable of cleaving double-stranded DNA and method of utilization of the same

INVENTOR(S): Sugiyama, Hiroshi; Tao, Zhi-Fu; Saito, Isao

PATENT ASSIGNEE(S): Japan Science and Technology Corporation, Japan

SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

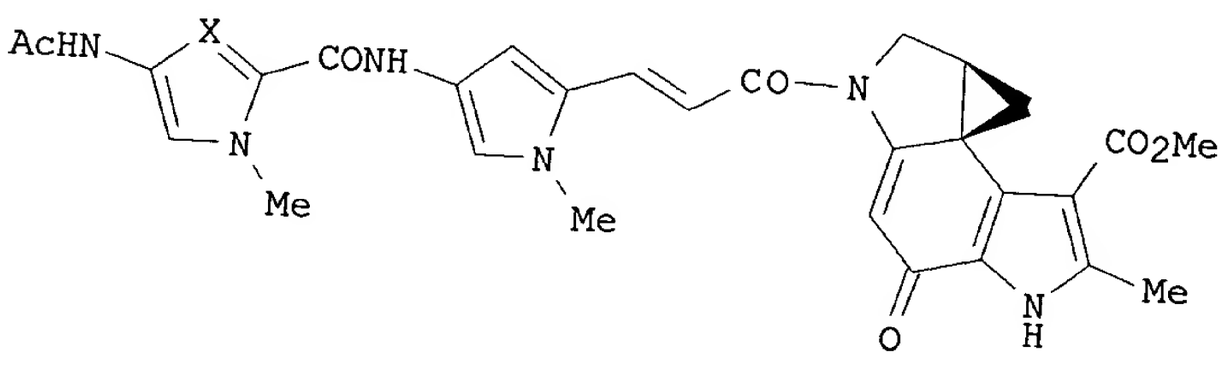
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058312	A1	20001005	WO 2000-JP1461	20000310
W: CA, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 2000281679	A2	20001010	JP 1999-83591	19990326
CA 2328903	AA	20001005	CA 2000-2328903	20000310
EP 1083177	A1	20010314	EP 2000-907992	20000310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

JP 1999-83591	A	19990326
WO 2000-JP1461	W	20000310

GI



I

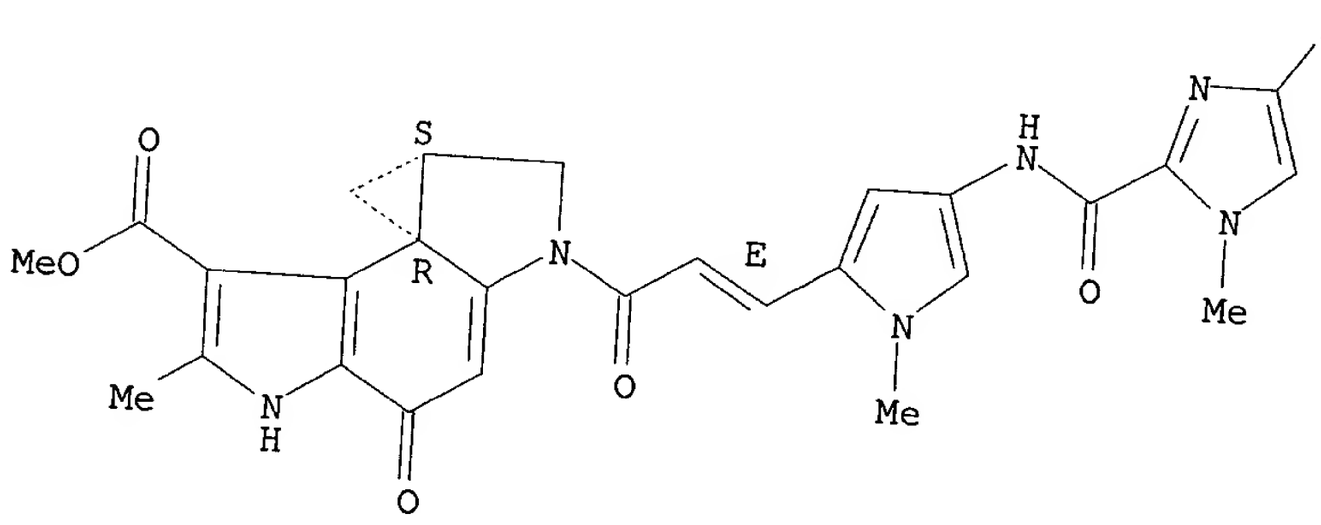
AB Novel chem. species represented by the following general formula B-L-A (I; wherein B represents a chem. structure capable of recognizing the base sequence of DNA, for example, optionally substituted pyrrole-imidazole polyamide; A represents a chem. structure capable of binding to one base of DNA, for example, the alkylation moiety of duocarmycin A; and L represents a linker capable of binding the chem. structures A and B, for example, vinyl) are prepd. Also claimed are a method for alkylating DNA and a method for cleaving double-stranded DNA by using these compds.; and medicinal compns. with the use of these compds. for treatment of cancer. These compds. I, e.g. duocarmycin derivs. (II; R = CH, N) (prepn. given) which recognizes base sequences TGACG or CGACG or their complimentary chain, are capable of simultaneously alkylating double-stranded DNA and cleaving the same and useful as artificial restriction enzymes or for targeting specific DNA base sequences for gene therapy. II (R = CH), II (R = N), and duocarmycin A in vitro showed IC50 of 1.5, 0.7 nM, and 4.7, resp., for inhibiting the proliferation of HeLaS3 cells.

IT **296794-37-1P 296794-38-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of duocarmycin derivs. capable of alkylating and cleaving double-stranded DNA as anticancer agents)

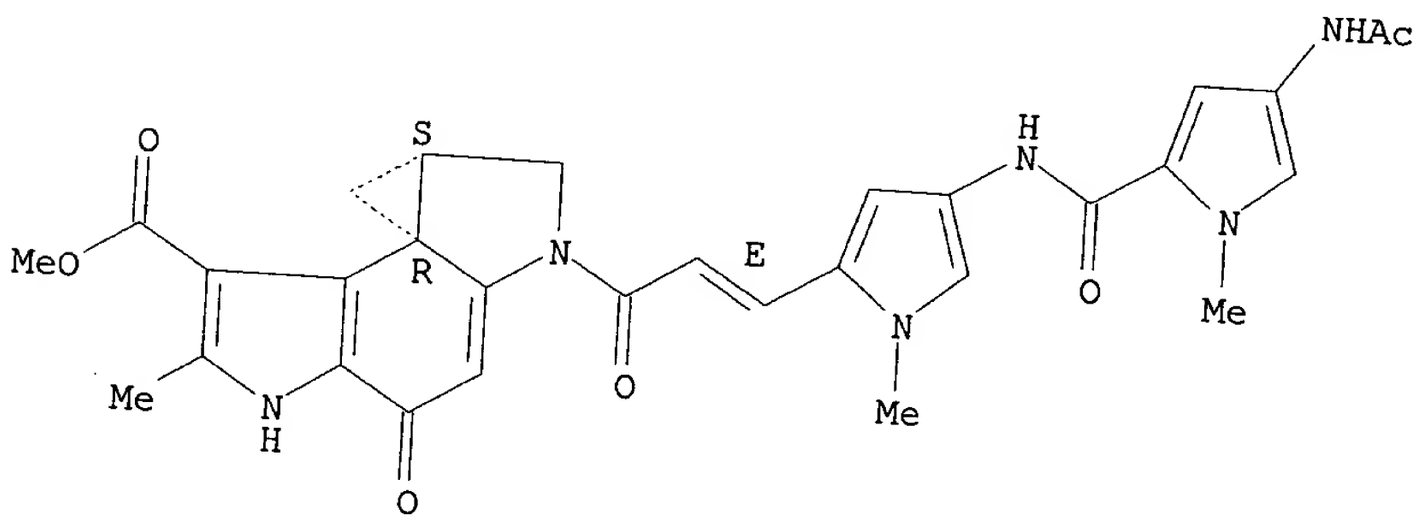
RN 296794-37-1 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[(2E)-3-[4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester, (7bR,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 296794-38-2 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[(2E)-3-[4-[[[4-(acetylamino)-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester, (7bR,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:96276 HCAPLUS

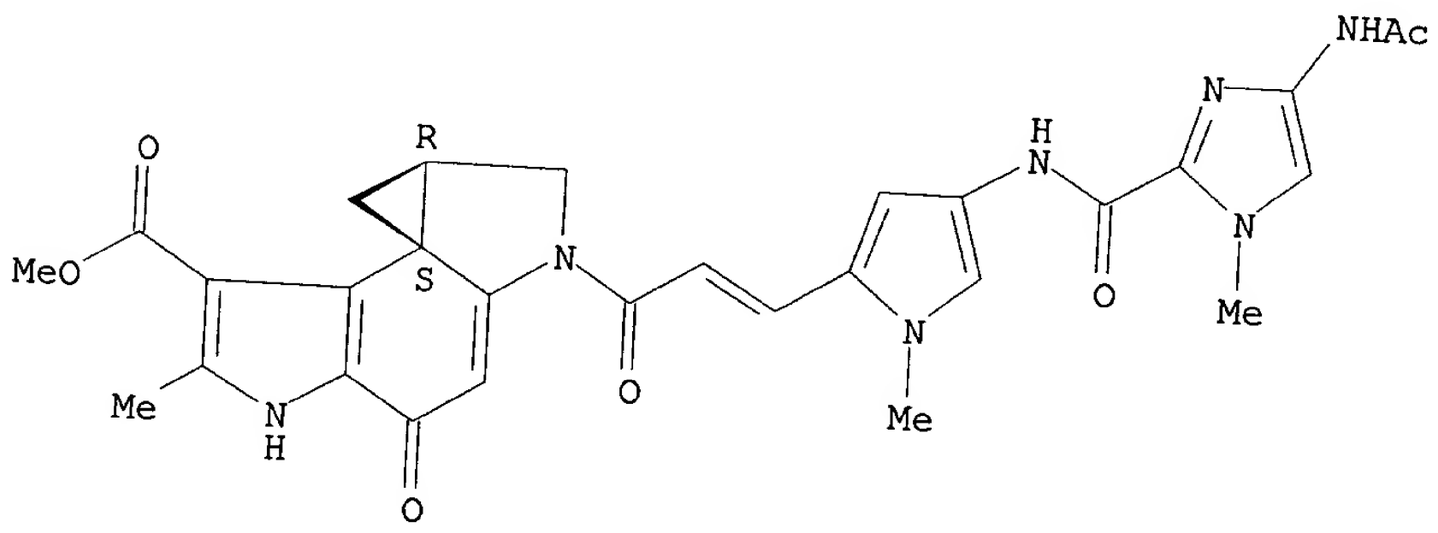
DOCUMENT NUMBER: 132:275556
TITLE: Highly cooperative DNA dialkylation by the homodimer of imidazole-pyrrole diamide-CPI conjugate with vinyl linker
AUTHOR(S): Tao, Zhi-Fu; Saito, Isao; Sugiyama, Hiroshi
CORPORATE SOURCE: CREST, Japan Science and Technology Corporation (JST), Japan
SOURCE: Journal of the American Chemical Society (2000), 122(8), 1602-1608
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:275556

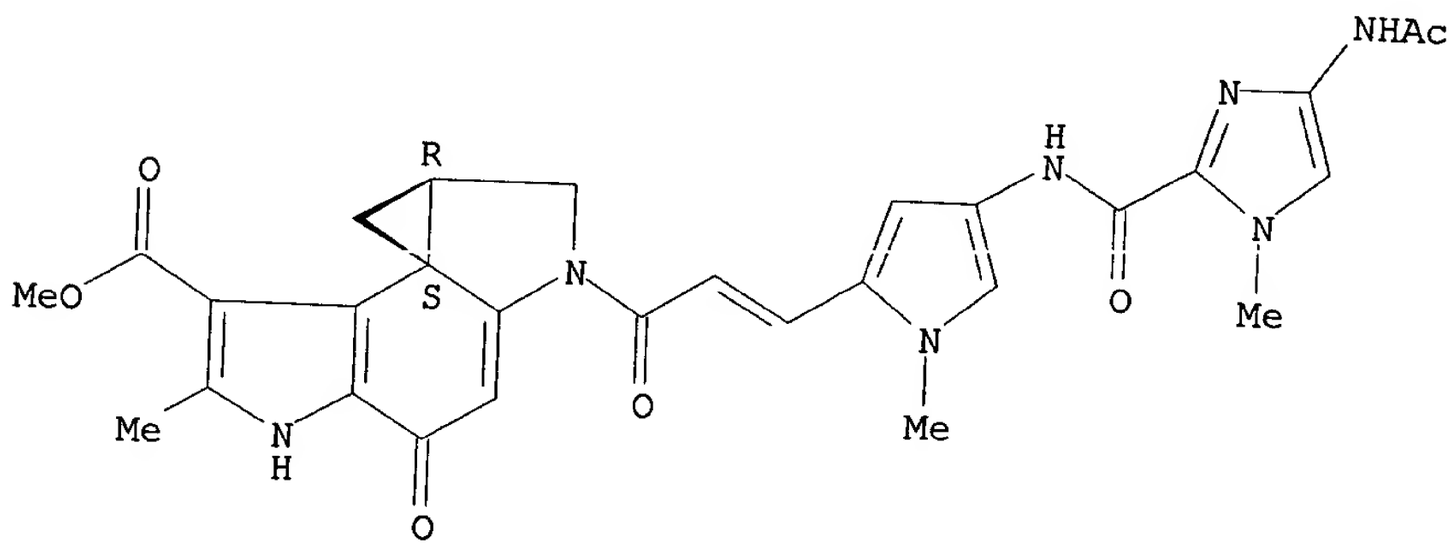
AB We synthesized new type of diamide-CPI conjugate possessing a vinyl linker (7). Sequence-selective alkylation of double-stranded DNA by 7 was investigated by high-resoln. denaturing gel electrophoresis using .apprx.400 bp DNA fragments. Highly efficient alkylation predominantly occurs simultaneously at the purines of 5'-PyG(A/T)CPu-3' site on both strands at a nanomolar concn. of 7. These results suggest that the homodimer of conjugate 7 dialkylates both strands according to Dervan's pairing rule together with a new mode of recognition in which the Im-vinyl linker (L) pair targets G/C base pairs. In addn. to the major dialkylation sites, a minor alkylation site was also obsd. at 5'-GT(A/T)GC-3'. This alkylation can be explained by an analogous slipped homodimer recognition mode in which the L-L pair recognizes the A/T base pair. Efficient dialkylation by the homodimer of 7 was further confirmed using oligonucleotides (ODNs). HPLC anal. revealed that the conjugate 7 simultaneously alkylates GN3/AN3 of the target sequences on both strands of ODNs.

IT **263710-69-6P**
RL: NUU (Other use, unclassified); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. and cooperative DNA dialkylation by imidazole-pyrrole diamide-CPI conjugate with vinyl linker)

RN 263710-69-6 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[3-[4-[[[4-(acetylamino)-1-methyl-1H-imidazol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester, (7bS,8aR)- (9CI) (CA INDEX NAME)

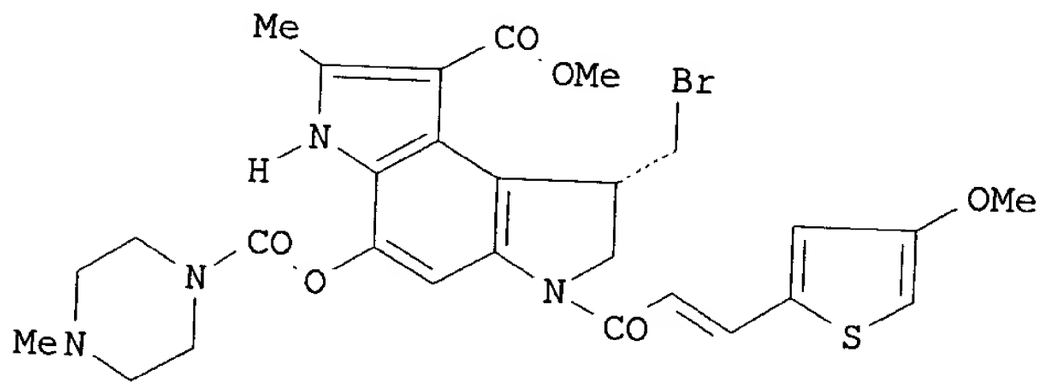
Absolute stereochemistry.
Double bond geometry unknown.





REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:674932 HCAPLUS
DOCUMENT NUMBER: 132:22791
TITLE: Synthesis and antitumor activity of duocarmycin derivatives: a-ring pyrrole compounds bearing 5-membered heteroarylacryloyl groups
AUTHOR(S): Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiji; Okamoto, Akihiko; Gomi, Katsushige; Saito, Hiromitsu
CORPORATE SOURCE: Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd., Shizuoka, 411-8731, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1999), 47(10), 1393-1403
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:22791
GI



I

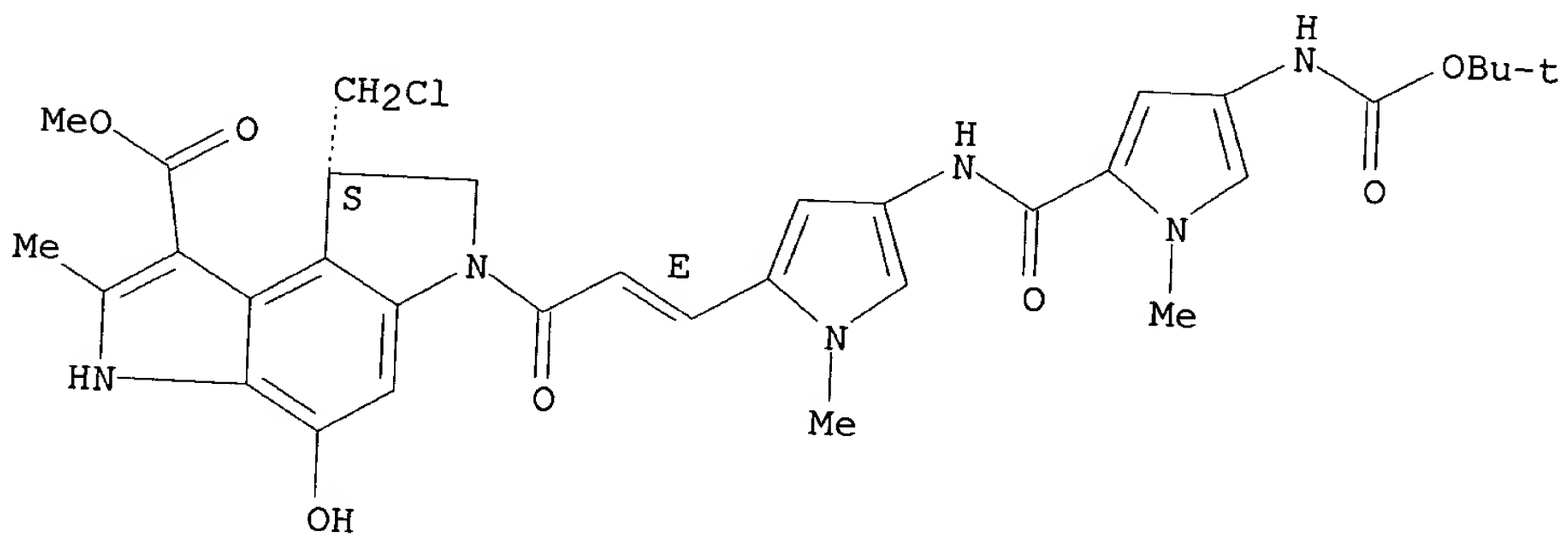
AB A series of A-ring pyrrole compds. of duocarmycin bearing 5-membered heteroarylacryloyl groups (thienylacryloyl and pyrrolylacryloyl) and heteroarylcarbonyl groups were synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. Most of the thienylacrylates displayed in vitro anticellular activity equiv. to 4'-methoxycinnamates.

Among the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of methoxy-thienylacrylates, compd. I, having 4'-methoxy-2'-thienylacryloyl as segment-B (Seg-B), showed remarkably potent antitumor activity and low peripheral blood toxicity in vivo, which were equal to those of 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxycinnamates, compared with the A-ring pyrrole derivs. having the trimethoxyindole skeleton in Seg-B. On the other hand, the 2'-pyrrolylacrylates having a double bond as spacer showed 102- to 103-fold stronger anticellular activity than 2'-pyrrolecarboxylates (IC50<0.3 nM, 72h-exposure). The 8-O-acetate and 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 2'-pyrrolylacrylates exhibited an antitumor effect at a lower dose compared with the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. with a 4'-methoxycinnamoyl moiety. Moreover, it was expected that the antitumor activity would be increased by the strength of the extra hydrogen bond formed between the nitrogen of the pyrrole amido group and DNA, owing to the increase of the no. of N-methyl-2'-pyrrolecarboxamide units. However, 2'-pyrrolylacrylates having three N-methyl-2'-pyrrolecarboxamide units showed nearly equal antitumor activity to 2'-pyrrolylacrylates having only one N-methyl-2'-pyrrolecarboxamide unit.

IT **251999-71-0P 251999-98-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of duocarmycin derivs. bearing 5-membered heteroarylacryloyl groups)

RN 251999-71-0 HCAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[(2E)-3-[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

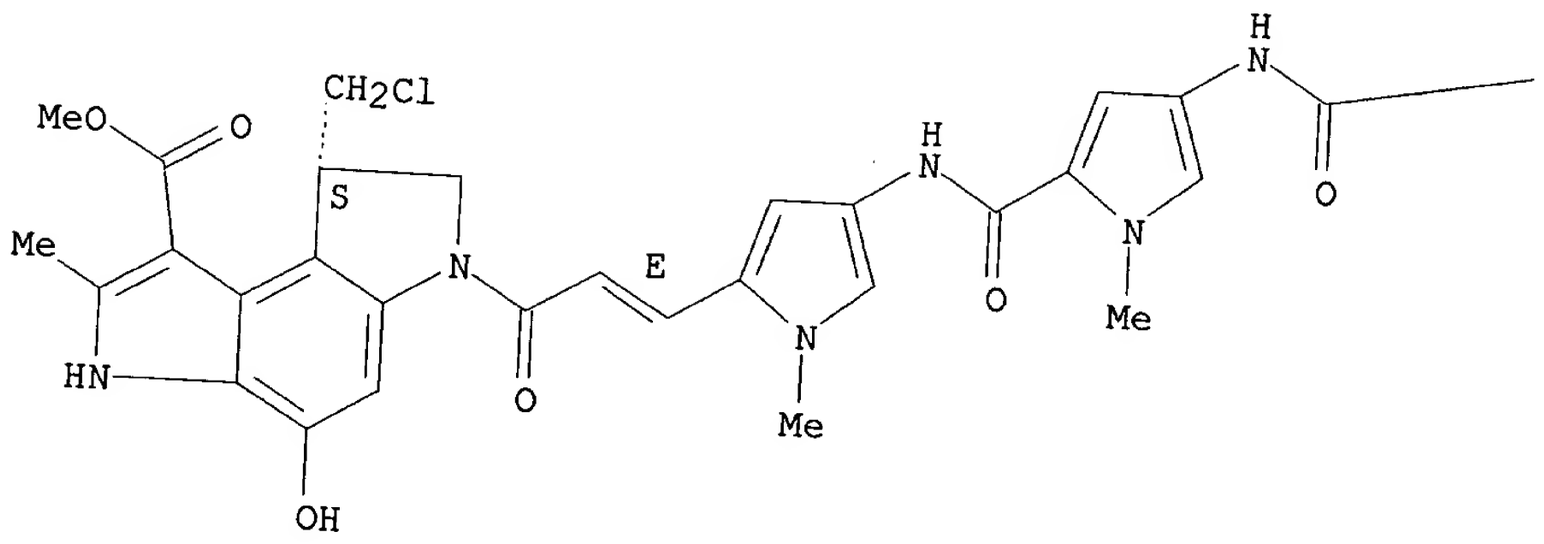


RN 251999-98-1 HCAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[(2E)-3-[4-[[[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-4-hydroxy-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

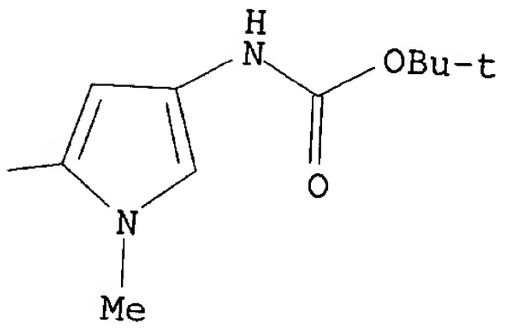
Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



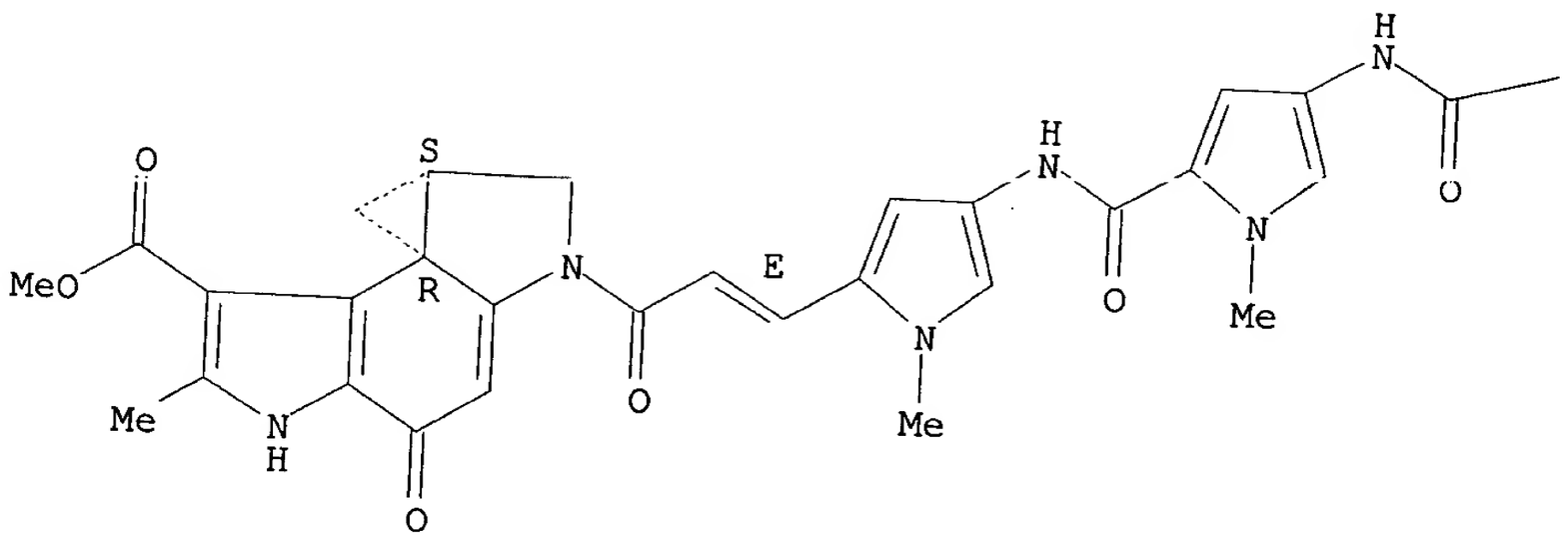
IT **251999-80-1P 251999-81-2P 251999-82-3P 251999-83-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of duocarmycin derivs. bearing 5-membered heteroarylacryloyl groups)

RN 251999-80-1 HCAPLUS

CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[(2E)-3-[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester, (7bR,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

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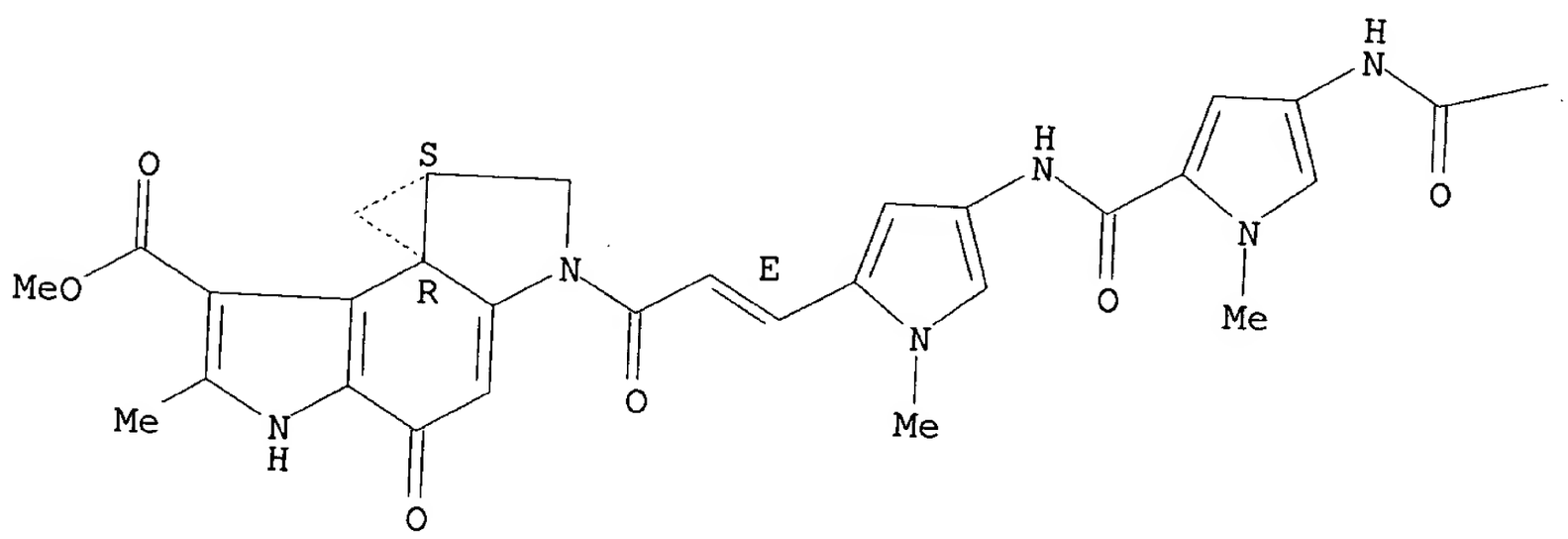
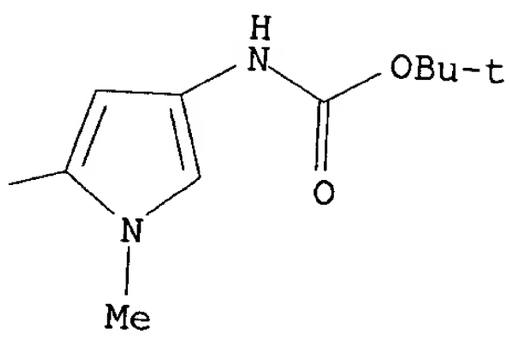
RN 251999-81-2 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[(2E)-3-[4-[[[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester, (7bR,8aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

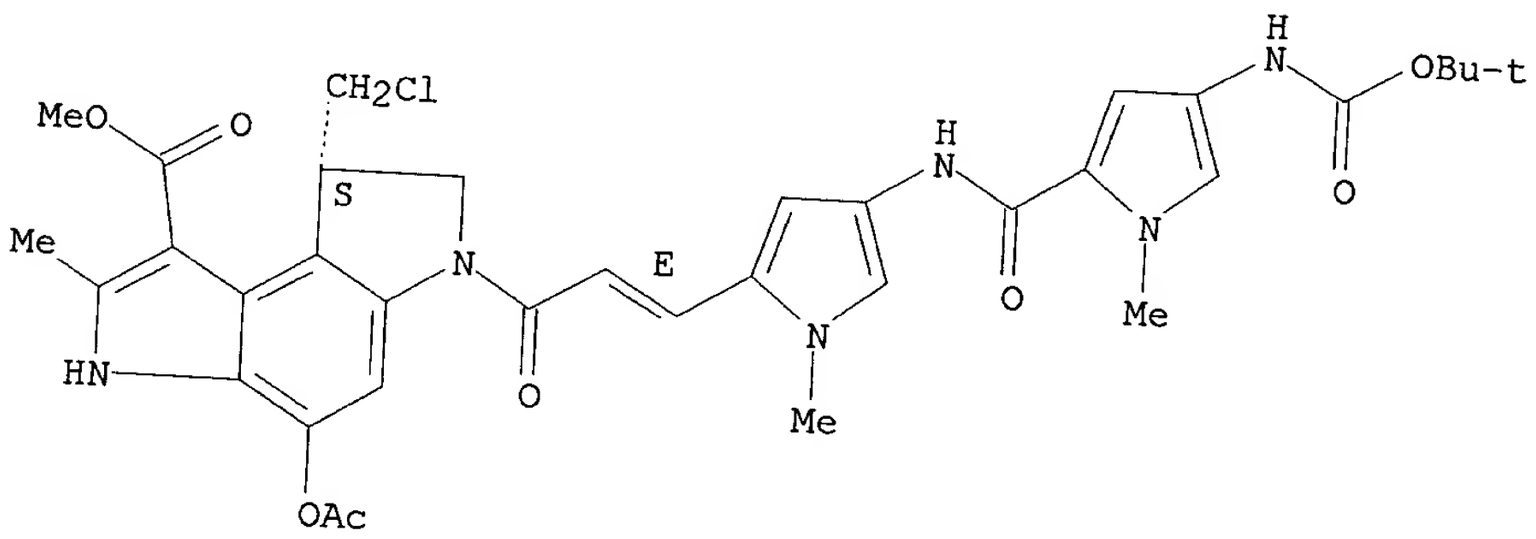
PAGE 1-A





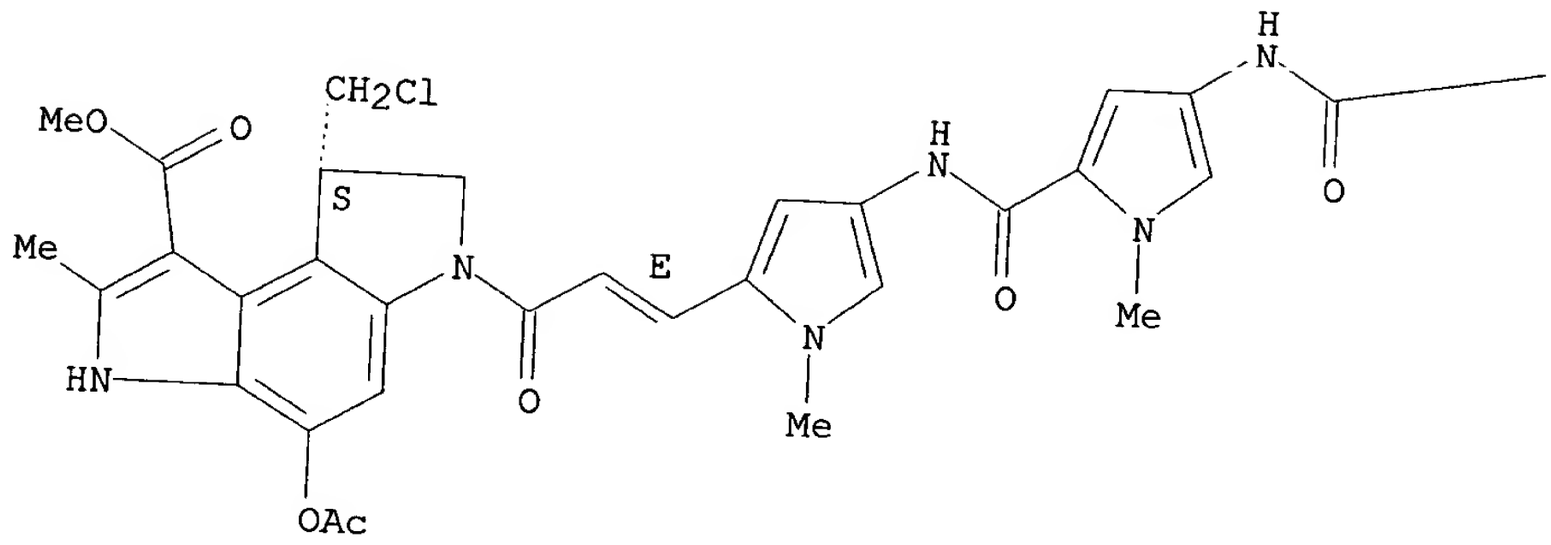
RN 251999-82-3 HCAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-6-[(2E)-3-[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

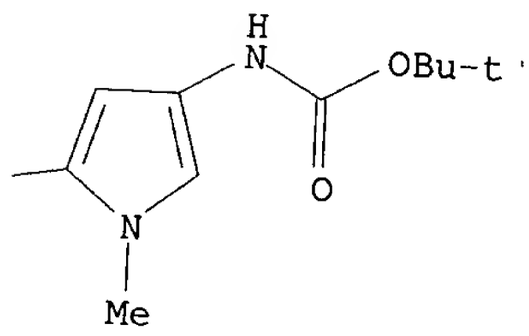
Absolute stereochemistry.
Double bond geometry as shown.



RN 251999-83-4 HCAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-6-[(2E)-3-[4-[[[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.





REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:87732 HCAPLUS
DOCUMENT NUMBER: 128:154100
TITLE: Preparation of DC-89 derivatives as antitumor agents
INVENTOR(S): Amishiro, Nobuyoshi; Saito, Hiromitsu; Okamoto, Akihiko; Gomi, Katsushige; Okabe, Masami
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan; Amishiro, Nobuyoshi; Saito, Hiromitsu; Okamoto, Akihiko; Gomi, Katsushige; Okabe, Masami
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803509	A1	19980129	WO 1997-JP2516	19970722
W: AU, BG, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

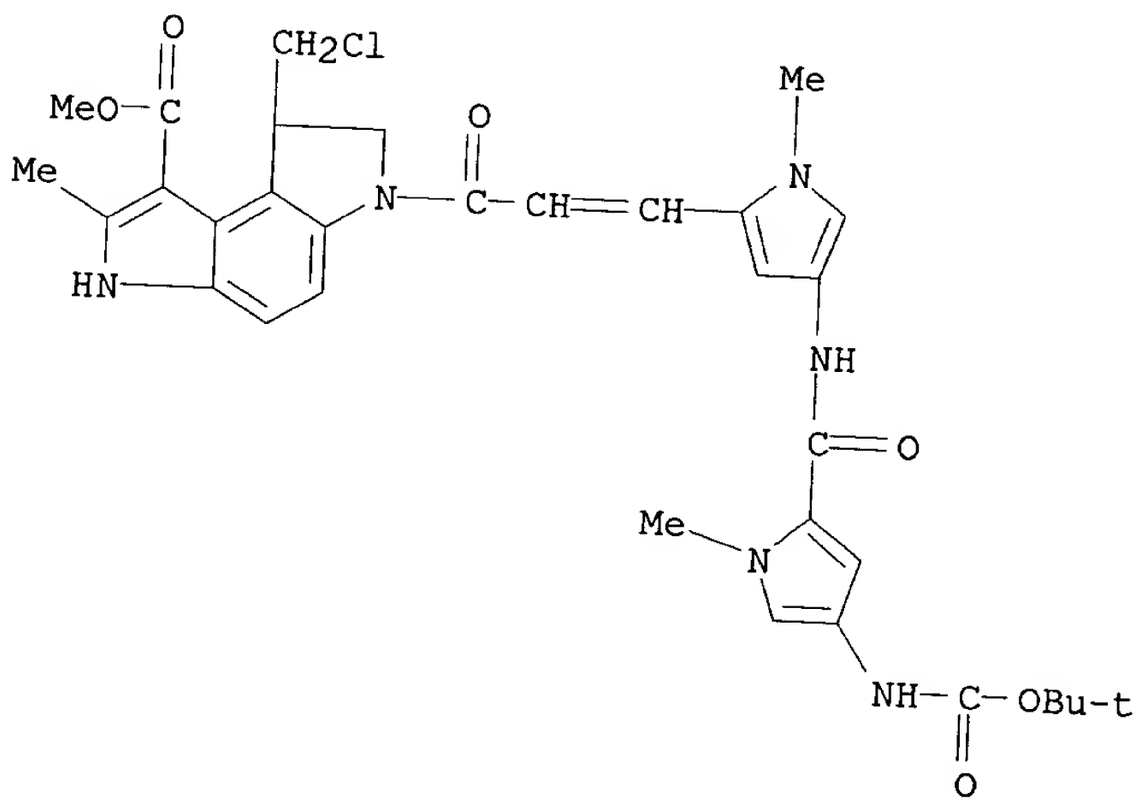
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AU 9734631 A1 19980210
PRIORITY APPLN. INFO.: AU 1997-34631 19970722
JP 1996-192634 19960723
WO 1997-JP2516 19970722
OTHER SOURCE(S): MARPAT 128:154100
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

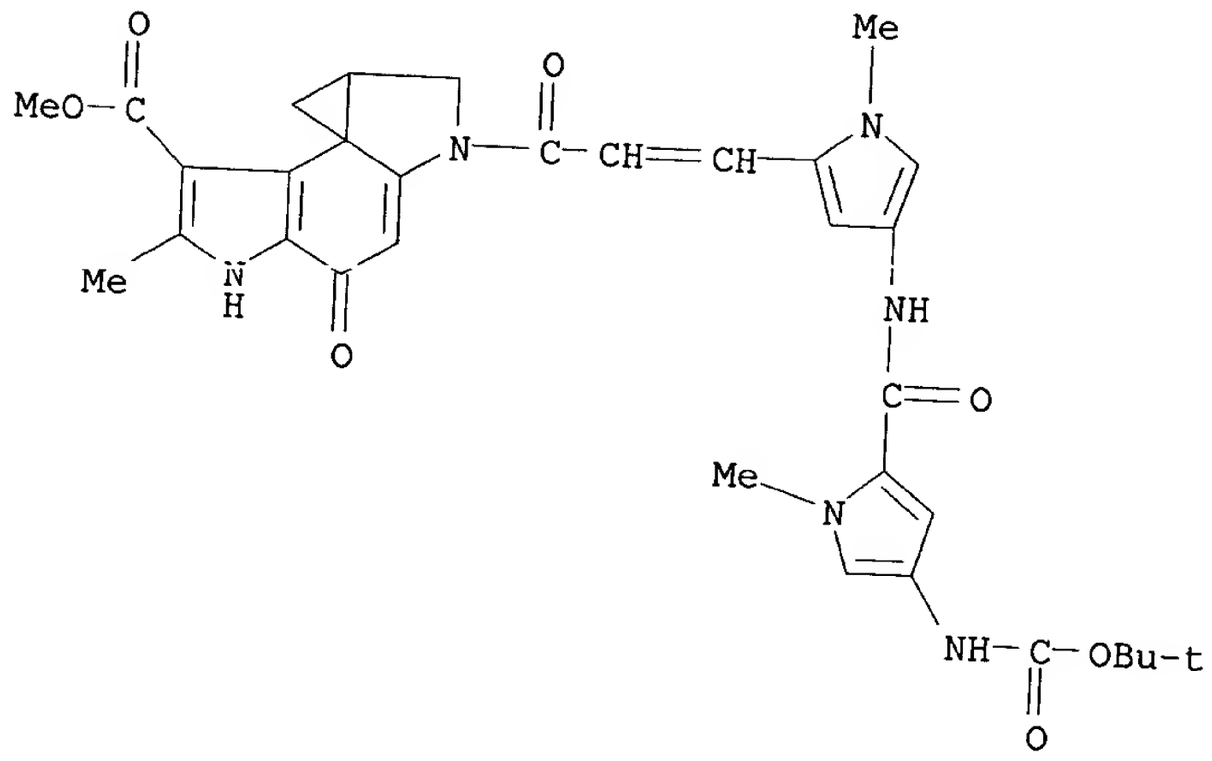
AB The title compds. (I) wherein (II) represents (III) or (IV) [X = Cl, Br; R = H, COR1, etc.; R1 = H, (un)substituted alkyl, etc.], and W represents (V) or (VI) (Y1, Y2 = O, S, etc.; Q1-Q5 = H, alkoxy, NO2, etc.; m = 0-1; n = 0-2), are prepd. I are useful as antitumor agents. Compd. (VII) was treated with NaH and then reacted with compd. (VIII) to give 73% the title compd. (IX), which showed IC50 of 2.9 nM against HeLaS3 cell.

IT **202419-11-2P 202419-12-3P 202419-13-4P**
202419-14-5P 202419-15-6P 202419-16-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of DC-89 derivs. as antitumor agents)

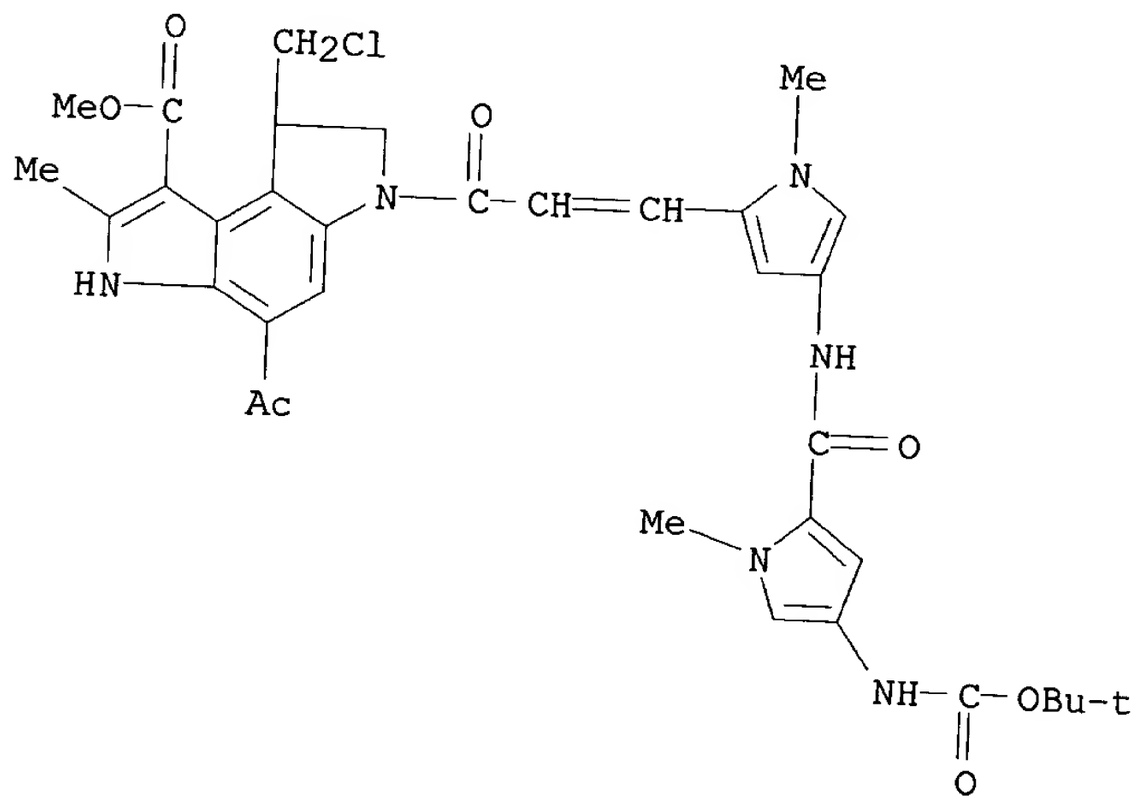
RN 202419-11-2 HCAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[3-[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6-dihydro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 202419-12-3 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[3-[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 202419-13-4 HCAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-acetyl-8-(chloromethyl)-6-[3-[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6-dihydro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 202419-14-5 HCAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[3-[4-[[[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6-dihydro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

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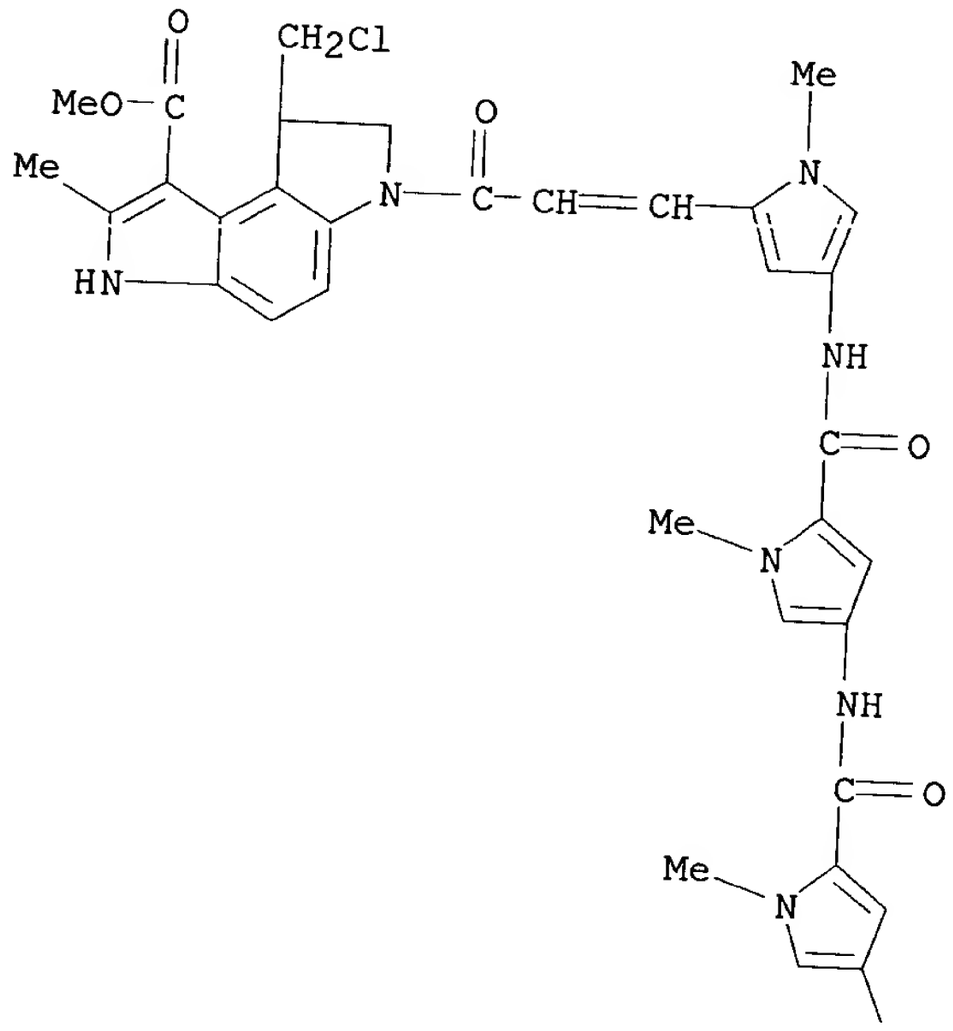
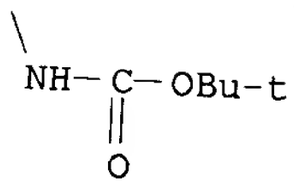


PAGE 2-A



RN 202419-15-6 HCAPLUS
CN Cyclopropa[c]pyrrolo[3,2-e]indole-7-carboxylic acid, 2-[3-[4-[[[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-1,2,4,5,8,8a-hexahydro-6-methyl-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

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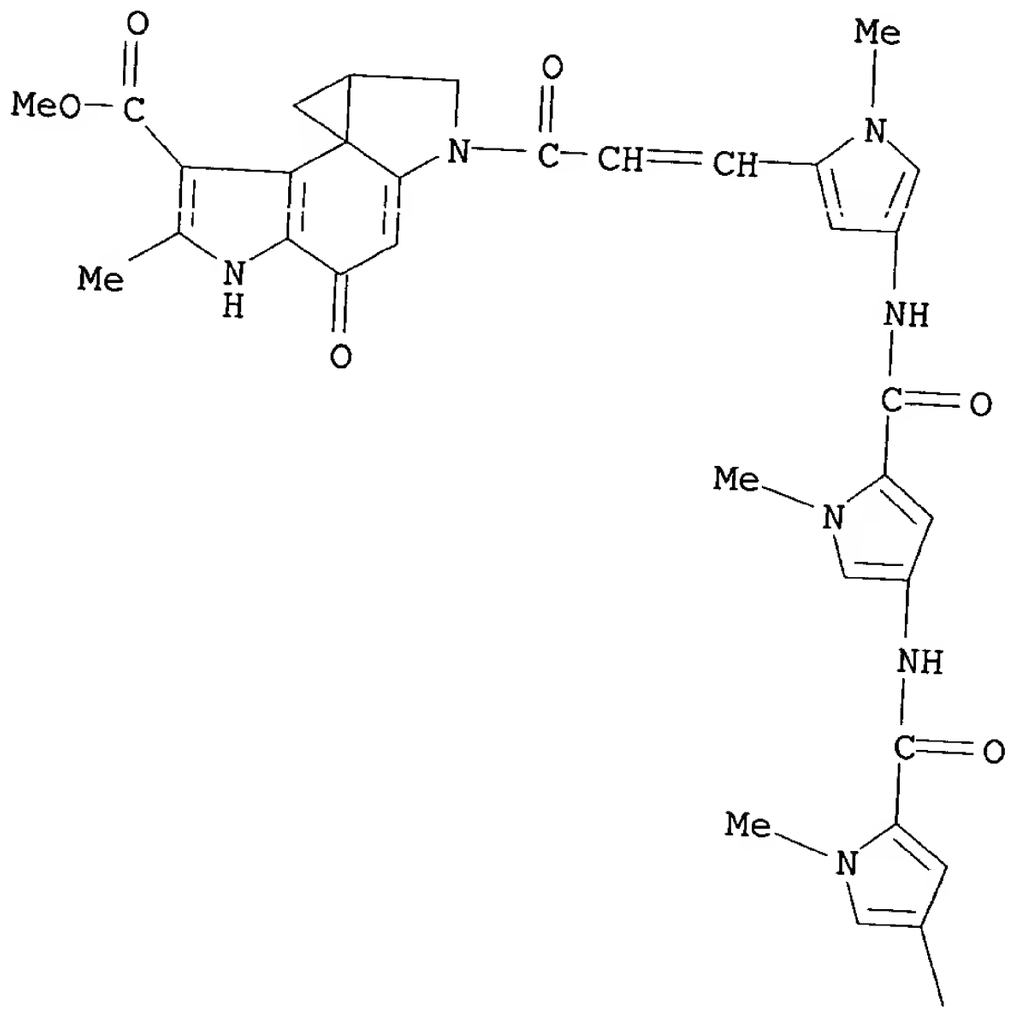
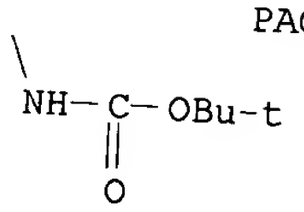
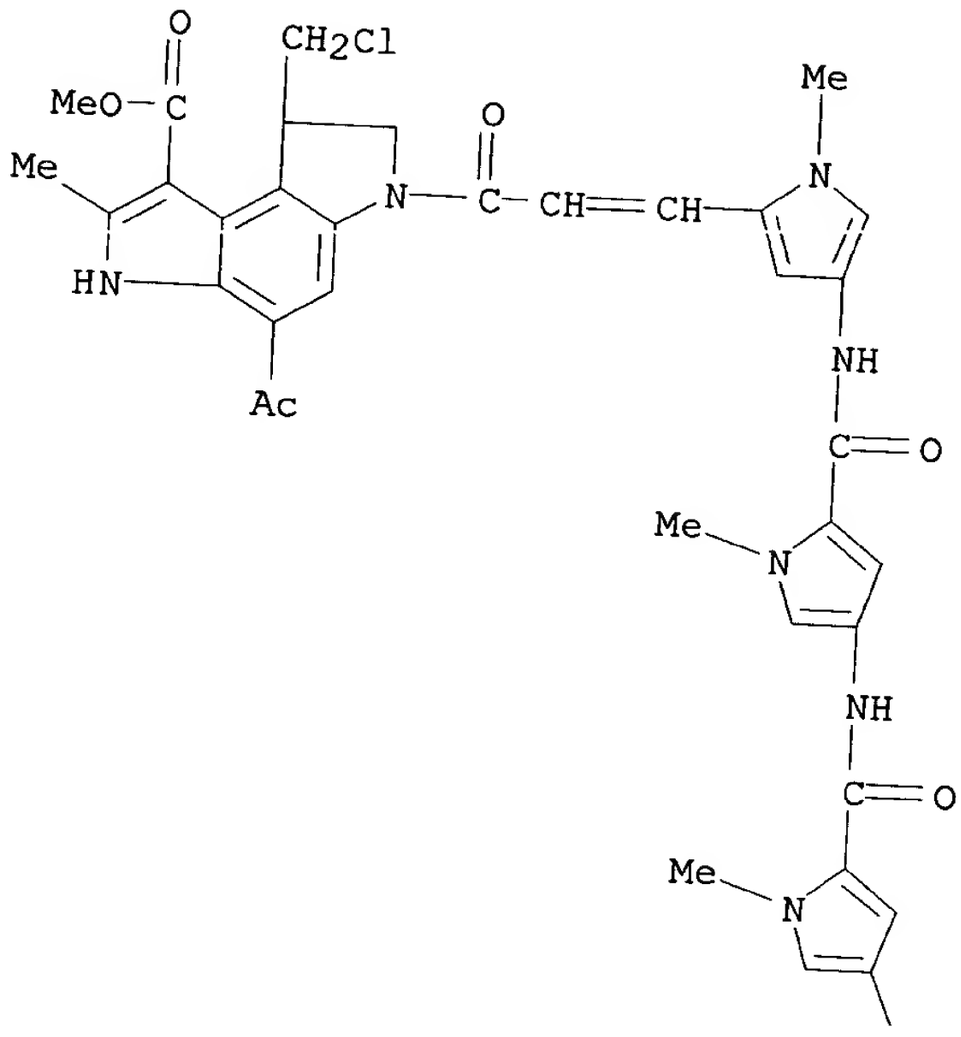


PAGE 2-A



RN 202419-16-7 HCAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-acetyl-8-(chloromethyl)-6-[3-[4-[[[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6-dihydro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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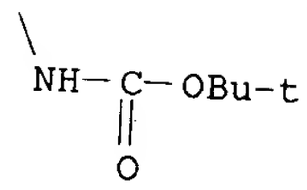


L4 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:783786 HCAPLUS
DOCUMENT NUMBER: 128:48468
TITLE: Preparation of DNA-binding glucuronide indoles immuno-conjugates as antitumors
INVENTOR(S): Wang, Yuqiang; Wright, Susan C.; Larrick, James W.
PATENT ASSIGNEE(S): Panorama Research, Inc., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744000	A2	19971127	WO 1997-US9055	19970522
WO 9744000	A3	19971231		

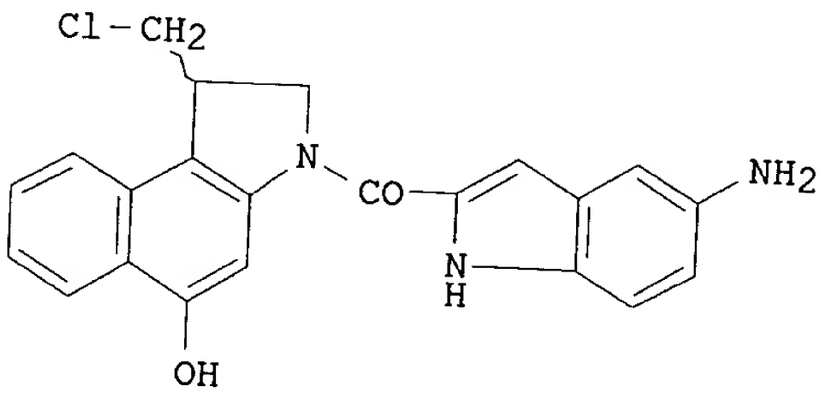
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,

LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN,
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG

US 5843937	A	19981201	US 1996-652883	19960523
AU 9732170	A1	19971209	AU 1997-32170	19970522
EP 918752	A2	19990602	EP 1997-927798	19970522
R: AT, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				
CN 1219841	A	19990616	CN 1997-194862	19970522
JP 2000511893	T2	20000912	JP 1997-542898	19970522

PRIORITY APPLN. INFO.: US 1996-652883 A 19960523
WO 1997-US9055 W 19970522

OTHER SOURCE(S): MARPAT 128:48468
GI

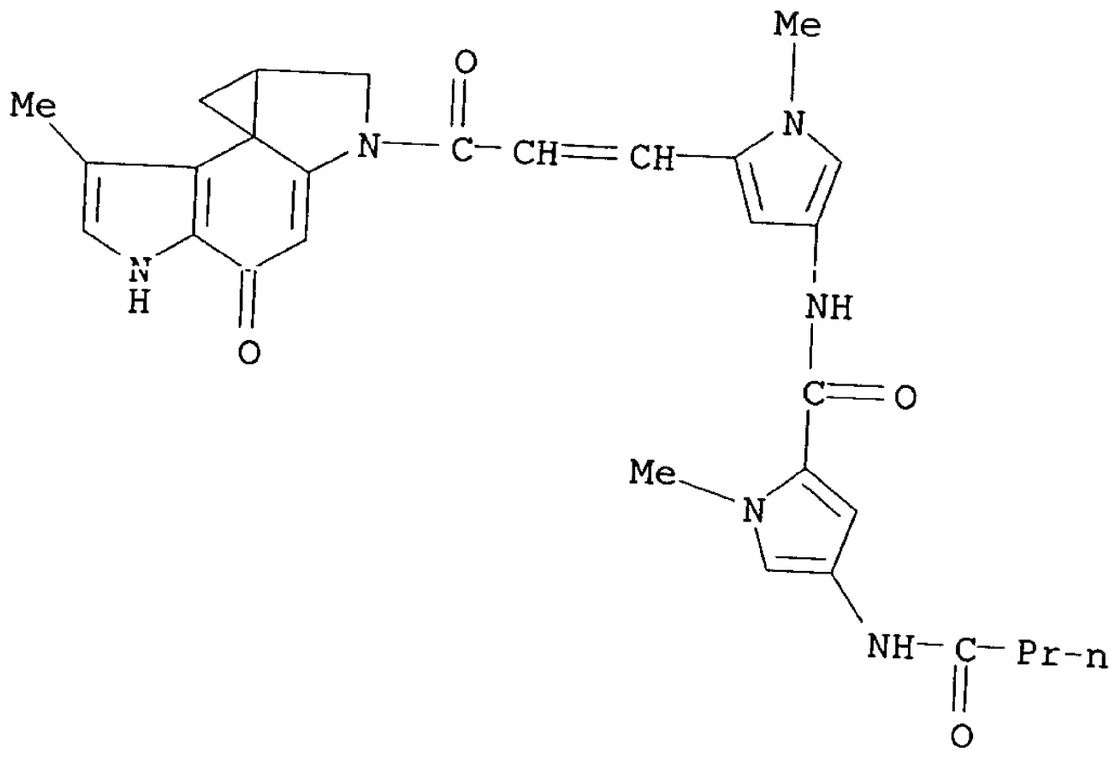


I

AB The present invention relates to novel DNA alkylating agents and the prodrugs of these agents which are useful as antitumors and DNA labeling agents. The compds. are hydroxydihydrobenzindole oligopeptides and prodrugs thereof wherein the monomeric constituents are derived from monocyclic, or bicyclic heterocyclic arom. residues. Thus, indole I was prepd. and tested for its antitumor activity with cytotoxicity (IC50 = 0.09 nM).

IT **199806-56-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)

RN 199806-56-9 HCAPLUS
CN 1H-Pyrrole-2-carboxamide, 1-methyl-N-[1-methyl-5-[3-oxo-3-(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)-1-propenyl]-1H-pyrrol-3-yl]-4-[(1-oxobutyl)amino]- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:248963 HCAPLUS
DOCUMENT NUMBER: 125:11480
TITLE: Cyclopropapyrroloindole-oligopeptide anticancer agents
INVENTOR(S): Lown, J. William; Wang, Yuqiang; Luo, Weide
PATENT ASSIGNEE(S): Synphar Laboratories, Inc., Can.
SOURCE: U.S., 17 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5502068	A	19960326	US 1995-381355	19950131
WO 9623497	A1	19960808	WO 1996-US727	19960131
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
CA 2210093	AA	19960808	CA 1996-2210093	19960131
AU 9649643	A1	19960821	AU 1996-49643	19960131
AU 698001	B2	19981022		
EP 800390	A1	19971015	EP 1996-906176	19960131
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 11500427	T2	19990112	JP 1996-523576	19960131

PRIORITY APPLN. INFO.: US 1995-381355 19950131
WO 1996-US727 19960131

OTHER SOURCE(S): MARPAT 125:11480
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is directed to novel cyclopropylpyrroloindole-oligopeptide compds. which are useful as anticancer agents. The novel cyclopropylpyrroloindole-oligopeptide compds. have the following general structure: I wherein, Het1 and Het2 are individually selected from the group consisting of pyrrole, imidazole, N-alkylimidazole, N-alkoxymethylimidazole, thiophene, thiophene, furan, thiazole, oxazole, N-alkylpyrrole, N-alkoxymethylpyrrole and pyrazole, R is selected from the group consisting of a valence bond; a divalent C1-C6 alkyl; a divalent C2-C6 alkenyl; a divalent C2-C6 alkynyl; a divalent cycloalkane of formula CpH2p-2 wherein p is 3 to 7; and an ortho, meta or para linked arom. group, A is selected from the group consisting of a C1-C6 alkyl group; an amidine or deriv. thereof; a guanidine; a secondary, tertiary or quaternary ammonium salt; and a sulfonium salt, n is 0 to 3, and m is 0 to 3, wherein when n=0, m is 1-3. Thus, e.g., deprotection of 5-benzyloxy-3-tert-butyloxycarbonyl-1-chloromethyl-8-methyl-1,2-dihydro-3H-pyrrolo[3,2-e]lindole (II) followed by coupling with 4-(4-butyramido-N-methyl-2-pyrrolecarboxyamido)-N-methyl-2-pyrroleacrylic acid and ring closure afforded (E)-1,2,8,8a-tetrahydro-7-methyl-2-[4-(4-butyramido-N-methyl-2-pyrrolecarboxyamido)-N-methyl-2-pyrroleacryloyl]cyclopropa[c]pyrrolo[3,2-e]indole-4-(5H)-one [(E)-III] which exhibited cytotoxicity of TD50 = 9.50 .times. 10-10 .mu.g/mL for KB human nasopharyngeal tumor cells (TD50 = 1 .times. 10-6 .mu.g/mL for CC-1065). A detailed anal. of the frequency of occurrence of bases flanking the prominent DNA alkylation sites for III is given and compared with CC-1065, providing evidence of the main cellular event that gives rise to the expression of anticancer properties of the new drugs and how they differ in detail from CC-1065.

IT **177177-55-8P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(cyclopropapyrroloindole-oligopeptide anticancer agents)

RN 177177-55-8 HCAPLUS

CN 1H-Pyrrole-2-carboxamide, 1-methyl-N-[1-methyl-5-[3-oxo-3-(4,5,8,8a-tetrahydro-7-methyl-4-oxocyclopropa[c]pyrrolo[3,2-e]indol-2(1H)-yl)-1-propenyl]-1H-pyrrol-3-yl]-4-[(1-oxobutyl)amino]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.